STIC SEARCH RESULTS

Biotech-Chem Library

Questions about the scope or the results of the search? Contact ***the searcher or contact:***

Mary Hale, Information Branch Supervisor
308-4258, CM1-1E01

Voluntary Results Feedback Form

- *I am an examiner in Workgroup:* ☐ *Example: 1610*
- *Relevant prior art **found**, search results used as follows:*
  - ☐ 102 rejection
  - ☐ 103 rejection
  - ☐ Cited as being of interest.
  - ☐ Helped examiner better understand the invention.
  - ☐ Helped examiner better understand the state of the art in their technology.

  Types of relevant prior art found:
  - ☐ Foreign Patent(s)
  - ☐ Non-Patent Literature
    (journal articles, conference proceedings, new product announcements etc.)
- *Relevant prior art **not found:***
  - ☐ Results verified the lack of relevant prior art (helped determine patentability).
  - ☐ Results were not useful in determining patentability or understanding the invention.

Comments:

Drop off or send completed forms to STIC/Biotech-Chem Library CM1 – Circ. Desk

Jan Delaval
Reference Librarian
Biotechnology & Chemical Library
CM1 1E07 – 703-308-4498
jan.delaval@uspto.gov

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=> d his

     (FILE 'HOME' ENTERED AT 15:17:42 ON 24 JUN 2003)
               SET COST OFF

     FILE 'REGISTRY' ENTERED AT 15:17:54 ON 24 JUN 2003
               E METOPROLOL/CN
L1             1 S E3
               SEL RN
L2            29 S E1/CRN
L3            17 S L2 NOT MXS/CI
L4           229 S C15H25NO3/MF AND 46.150.18/RID AND 1/NR
L5            17 S L4 AND 2 PROPANOL AND 2 METHOXYETHYL PHENOXY
L6            13 S L5 NOT (D OR T)/ELS
L7             7 S L6 AND 4
               SEL RN
L8            14 S E2-E8/CRN NOT L2
L9            13 S L8 NOT MXS/CI
L10            7 S L9 NOT COMPD
L11           31 S L1,L3,L7,L10
L12           22 S L11 NOT (COMPD OR WITH)
L13           21 S L12 NOT 11C
L14           10 S L11 NOT L13

     FILE 'HCAPLUS' ENTERED AT 15:23:45 ON 24 JUN 2003
L15         2799 S L13
L16         3247 S METOPROLOL OR BEATROLOL OR SPESICOR OR CGP2175 OR CGP 2175
L17         3560 S L15,L16
               E ALEXANDER J/AU
L18          320 S E3,E8-E10
               E ALEXANDER JOHN/AU
L19           29 S E3,E10-E12
               E SCHUH J/AU
L20           53 S E3,E6,E14,E17,E18,E21,E22
L21            1 S L17 AND L18-L20

     FILE 'REGISTRY' ENTERED AT 15:25:56 ON 24 JUN 2003
L22            1 S EPLERENONE/CN
L23           36 S 107724-20-9/CRN

     FILE 'HCAPLUS' ENTERED AT 15:27:15 ON 24 JUN 2003
L24           67 S L22
L25            8 S L23
L26           81 S EPLERENONE OR SC66110 OR SC()(66110 OR 66 110) OR CGP30083 OR
L27           92 S L24-L26
L28            7 S L27 AND L18-L20
L29            1 S L21 AND L28
L30            1 S US20020123485/PN
               E WO2001-US23670/AP,PRN
L31            1 S E3,E4
               E US2000-221365/AP,PRN
L32            1 S E5
L33            1 S L29-L32
               SEL RN

     FILE 'REGISTRY' ENTERED AT 15:29:09 ON 24 JUN 2003
L34           80 S E1-E80
L35            2 S L34 AND L22,L23
L36            1 S L34 AND L13
L37           16 S L34 AND NR>=5
L38           12 S L34 AND NR>=6
L39           16 S L37,L38
L40           63 S L34 NOT L35-L39
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L41             3 S L39 AND K/ELS
L42            11 S L38 NOT L41
L43            10 S L42 AND 1/NC
L44               STR
L45            50 S L44
L46               STR L44
L47            18 S L46
L48               STR L46
L49            50 S L48
L50               SCR 1851
L51            50 S L48 AND L50
L52          1341 S L48 AND L50 FUL
                  SAV L52 QAZI917/A
L53               STR
L54            22 S L53 SAM SUB=L52
L55            10 S L34 AND L52
L56             6 S L39 NOT L55
L57           554 S L53 FUL SUB=L52
                  SAV L57 QAZI917A/A
L58           552 S L57 NOT (CCS OR RIS OR PMS)/CI

     FILE 'HCAPLUS' ENTERED AT 15:52:30 ON 24 JUN 2003
L59            67 S L55
L60             4 S L59 AND L17

     FILE 'REGISTRY' ENTERED AT 15:53:12 ON 24 JUN 2003
L61             5 S L56 NOT C24H32O4S

     FILE 'HCAPLUS' ENTERED AT 15:53:50 ON 24 JUN 2003
L62             2 S L61
L63             1 S L62 AND L17
L64             4 S L27 AND L17
L65             4 S L33,L60,L63,L64
L66           360 S L58
L67             4 S L66 AND L17
L68             4 S L65,L67

=> fil reg
FILE 'REGISTRY' ENTERED AT 15:56:48 ON 24 JUN 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2003 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:   23 JUN 2003  HIGHEST RN 536496-82-9
DICTIONARY FILE UPDATES:  23 JUN 2003  HIGHEST RN 536496-82-9

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2003

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available.  See HELP
PROPERTIES for more information.  See STNote 27, Searching Properties
in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=> d sta que l57
L48             STR
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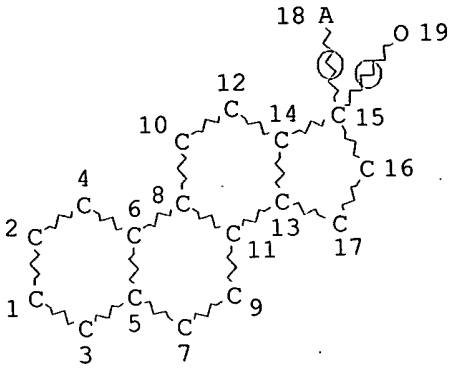
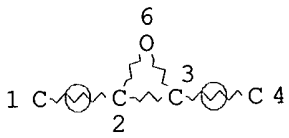


NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 19

STEREO ATTRIBUTES: NONE
L50 SCR 1851
L52 1341 SEA FILE=REGISTRY SSS FUL L48 AND L50
L53 STR



NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 5

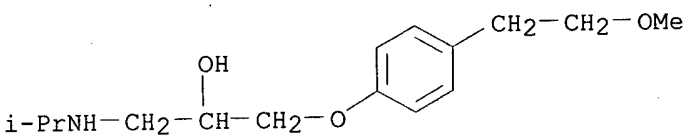
STEREO ATTRIBUTES: NONE
L57 554 SEA FILE=REGISTRY SUB=L52 SSS FUL L53

100.0% PROCESSED 607 ITERATIONS 554 ANSWERS
SEARCH TIME: 00.00.01

=> d ide can l1

L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS
RN 51384-51-1 REGISTRY
CN 2-Propanol, 1-[4-(2-methoxyethyl)phenoxy]-3-[(1-methylethyl)amino]- (9CI)
(CA INDEX NAME)
OTHER NAMES:
CN (.+-.)-Metoprolol
CN (RS)-Metoprolol
CN 1-Isopropylamino-3-[4-(2-methoxyethyl)phenoxy]-2-propanol
CN Beatrolol
CN CGP 2175
CN dl-Metoprolol

CN **Metoprolol**
CN Spesicor
FS 3D CONCORD
DR 54163-88-1, 37350-58-6
MF C15 H25 N O3
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMLIST, CIN, CSCHEM, DDFU, DIOGENES, DRUGPAT, DRUGU, EMBASE, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, NIOSHTIC, PHAR, PHARMASEARCH, PROMT, RTECS*, SPECINFO, TOXCENTER, ULIDAT, USAN, USPAT2, USPATFULL, VETU
(*File contains numerically searchable property data)
Other Sources: EINECS**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2327 REFERENCES IN FILE CA (1957 TO DATE)
29 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
2329 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 138:406708

REFERENCE 2: 138:396171

REFERENCE 3: 138:395842

REFERENCE 4: 138:378918

REFERENCE 5: 138:378518

REFERENCE 6: 138:378466

REFERENCE 7: 138:373982

REFERENCE 8: 138:362715

REFERENCE 9: 138:362688

REFERENCE 10: 138:362127

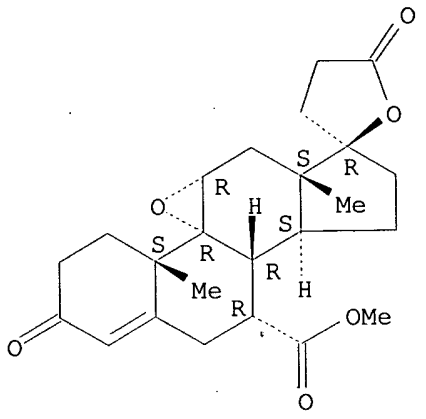
=> d ide can 122

L22 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS
RN 107724-20-9 REGISTRY
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, .gamma.-lactone, methyl ester, (7.alpha.,11.alpha.,17.alpha.)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Spiro[9,11-epoxy-9H-cyclopenta[a]phenanthrene-17(2H),2'(3'H)-furan],

pregn-4-ene-7,21-dicarboxylic acid deriv.

OTHER NAMES:
CN CGP 30083
CN **Eplerenone**
CN SC 66110
FS STEREOSEARCH
MF C24 H30 O6
CI COM
SR CA
LC STN Files: ADISINSIGHT, ADISNEWS, ANABSTR, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CIN, DDFU, DIOGENES, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, IPA, MEDLINE, PHAR, PROMT, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

67 REFERENCES IN FILE CA (1957 TO DATE)
4 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
69 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 138:395116

REFERENCE 2: 138:363210

REFERENCE 3: 138:362110

REFERENCE 4: 138:343856

REFERENCE 5: 138:335571

REFERENCE 6: 138:296950

REFERENCE 7: 138:202478

REFERENCE 8: 138:163269

REFERENCE 9: 138:134888

REFERENCE 10: 138:126982

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=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 15:57:22 ON 24 JUN 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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FILE COVERS 1907 - 24 Jun 2003  VOL 138 ISS 26
FILE LAST UPDATED: 23 Jun 2003  (20030623/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.


=> d all hitstr tot 168

L68  ANSWER 1 OF 4  HCAPLUS  COPYRIGHT 2003 ACS
AN   2003:319257  HCAPLUS
DN   138:343856
TI   Buccal sprays or capsules containing cardiovascular or renal drugs
IN   Dugger, Harry A.
PA   USA
SO   U.S. Pat. Appl. Publ., 15 pp., Cont.-in-part of U.S. Ser. No. 537,118.
     CODEN: USXXCO
DT   Patent
LA   English
IC   ICM  A61K009-00
     ICS  A61L009-04
NCL  424043000
CC   63-6 (Pharmaceuticals)
FAN.CNT 8
     PATENT NO.          KIND  DATE          APPLICATION NO.  DATE
     ---------------     ----  --------      ---------------  --------
PI   US 2003077229       A1    20030424      US 2002-230075   20020829
     WO 9916417          A1    19990408      WO 1997-US17899  19971001
         W:  AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
             DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ,
             LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL,
             PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US,
             UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR,
             GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA,
             GN, ML, MR, NE, SN, TD, TG
     EP 1029536          A1    20000823      EP 2000-109347   19971001
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             IE, SI, LT, LV, FI, RO
     EP 1036561          A1    20000920      EP 2000-109357   19971001
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO
PRAI WO 1997-US17899     A2    19971001
     US 2000-537118      A2    20000329
     EP 1997-911621      A3    19971001
AB   Buccal aerosol sprays or capsules using polar and non-polar solvent have
```

now been developed which provide biol. active compds. for rapid absorption through the oral mucosa, resulting in fast onset of effect. The buccal polar compns. of the invention comprise formulation A: aq. polar solvent, active compd., and optional flavoring agent; formulation B: aq. polar solvent, active compd., optionally flavoring agent, and propellant; formulation C: non-polar solvent, active compd., and optional flavoring agent; and formulation D: non-polar solvent, active compd., optional flavoring agent, and propellant. Thus, a polar lingual spray contained isoproterenol-HCl 0.5-6, water 50-75, EtOH 5-10, PEG 5-15, sorbitol 0.4-1.0, aspartame 0.04-0.1, and flavors 2-3%.

ST cardiovascular drug buccal spray; renal drug capsule

IT Fatty acids, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(C2-24; buccal sprays or capsules contg. cardiovascular or renal drugs)

IT Alcohols, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(C2-8; buccal sprays or capsules contg. cardiovascular or renal drugs)

IT Alcohols, biological studies
Hydrocarbons, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(C7-18; buccal sprays or capsules contg. cardiovascular or renal drugs)

IT Drug delivery systems
(aerosols, sprays; buccal sprays or capsules contg. cardiovascular or renal drugs)

IT Antianginal agents
Antiarrhythmics
Anticoagulants
Antihypertensives
Antihypotensives
Cardiovascular agents
Flavor
Polar solvents
Propellants (sprays and foams)
Sweetening agents
Vasodilators
(buccal sprays or capsules contg. cardiovascular or renal drugs)

IT Esters, biological studies
Glycerides, biological studies
Pentosans
Polyoxyalkylenes, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(buccal sprays or capsules contg. cardiovascular or renal drugs)

IT Drug delivery systems
(buccal; buccal sprays or capsules contg. cardiovascular or renal drugs)

IT Drug delivery systems
(capsules; buccal sprays or capsules contg. cardiovascular or renal drugs)

IT Essential oils
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(citrus; buccal sprays or capsules contg. cardiovascular or renal drugs)

IT Heart, disease
(failure; buccal sprays or capsules contg. cardiovascular or renal drugs)

IT Flavoring materials
(fruit flavors; buccal sprays or capsules contg. cardiovascular or renal drugs)

IT Mucopolysaccharides, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(heparinoids; buccal sprays or capsules contg. cardiovascular or renal drugs)

IT Peptides, biological studies.

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(hormones; buccal sprays or capsules contg. cardiovascular or renal drugs)

IT Mouth
(mucosa; buccal sprays or capsules contg. cardiovascular or renal drugs)

IT Drug delivery systems
(mucosal; buccal sprays or capsules contg. cardiovascular or renal drugs)

IT Essential oils
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(peppermint; buccal sprays or capsules contg. cardiovascular or renal drugs)

IT Hormones, animal, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(peptide; buccal sprays or capsules contg. cardiovascular or renal drugs)

IT Alcohols, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polyhydric, C2-8; buccal sprays or capsules contg. cardiovascular or renal drugs)

IT Heart
(regulators for; buccal sprays or capsules contg. cardiovascular or renal drugs)

IT Essential oils
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(spearmint; buccal sprays or capsules contg. cardiovascular or renal drugs)

IT Drug delivery systems
(sprays; buccal sprays or capsules contg. cardiovascular or renal drugs)

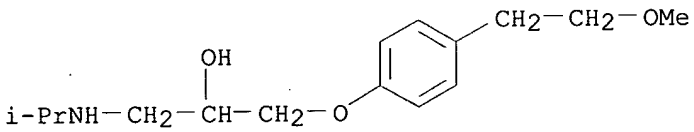
IT 9005-49-6, Heparin, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(SNAC/SNAD; buccal sprays or capsules contg. cardiovascular or renal drugs)

IT 50-78-2, Aspirin 51-06-9, Procainamide 51-30-9, Isoproterenol hydrochloride 54-31-9, Furosemide 56-54-2, Quinidine 57-41-0, Phenytoin 58-00-4, Apomorphine 58-32-2, Dipyridamole 58-54-8, Ethacrynic acid 58-55-9, Theophylline, biological studies 58-61-7, Adenosine, biological studies 59-41-6, Bretylium 60-87-7, Promethazine 64-17-5, Ethanol, biological studies 65-28-1, Phentolamine mesylate 71-63-6, Digitoxin 74-98-6, Propane, biological studies 75-28-5, Iso-butane 78-11-5, Pentaerythritol tetranitrate 78-78-4, Iso-pentane 81-81-2, Warfarin 86-54-4, Hydralazine 87-33-2, Isosorbide dinitrate 89-25-8, Edaravone 106-97-8, N-Butane, biological studies 109-66-0, N-Pentane, biological studies 114-07-8, Erythromycin 127-31-1, Fludrocortisone 137-58-6, Lidocaine 147-24-0, DiPhenhydramine hydrochloride 303-53-7, Cyclobenzaprine 364-98-7, Diazoxide 463-04-7, Amyl nitrite 463-82-1, Neo-pentane 523-87-5, Dimenhydrinate 525-66-6, Propranolol 541-15-1, Carnitine 555-30-6, Methyldopa 569-65-3, Meclizine 630-93-3, Phenytoin sodium 745-65-3, Alprostadil 1951-25-3, Amiodarone 3239-44-9, Dexfenfluramine 3737-09-5, Disopyramide 3930-20-9, Sotalol 4205-90-7, Clonidine 5786-21-0, Clozapine 6493-05-6, Pentoxifylline 7297-25-8, Erythrityl tetranitrate 9041-08-1 10238-21-8, Glyburide 13523-86-9, Pindolol 15078-28-1, Nitroprusside 19216-56-9, Prazosin 20830-75-5, Digoxin 21829-25-4, Nifedipine 23031-25-6, Terbutaline 23031-32-5, Terbutaline sulfate 25322-68-3, Polyethylene glycol 25717-80-0, Molsidomine 28395-03-1, Bumetanide 29110-47-2, Guanfacine 29122-68-7, Atenolol 30236-31-8, D-Sotalol 30516-87-1, Zidovudine 31329-57-4, Naftidrofuryl 31828-71-4, Mexiletine 34368-04-2, Dobutamine 35700-23-3, Carboprost 36894-69-6, Labetalol 37270-89-6, Nadroparin calcium 37517-30-9, Acebutolol 38304-91-5, Minoxidil 39562-70-4, Nitrendipine

41708-72-9, Tocainide 42200-33-9, Nadolol 42399-41-7, Diltiazem
42794-76-3, Midodrine 47931-85-1, Salmon calcitonin 49562-28-9,
Fenofibrate **51384-51-1, Metoprolol** 54063-53-5,
Propafenone 54143-55-4, Flecainide 55142-85-3, Ticlopidine
55837-25-7, Buflomedil 55985-32-5, Nicardipine 56211-40-6, Torsemide
56980-93-9, Celiprolol 62571-86-2, Captopril 63590-64-7, Terazosin
63659-18-7, Betaxolol 63675-72-9, Nisoldipine 64706-54-3, Bepridil
65141-46-0, Nicorandil 66085-59-4, Nimodipine 66722-44-9, Bisoprolol
67227-56-9, Fenoldopam 70059-30-2, Cimetidine hydrochloride
72509-76-3, Felodipine 72956-09-3, Carvedilol 73963-72-1, Cilostazol
74191-85-8, Doxazosin 74863-84-6, Argatroban 75438-57-2, Moxonidine
75695-93-1, Isradipine 75847-73-3, Enalapril 76547-98-3, Lisinopril
76824-35-6, Famotidine 78415-72-2, Milrinone 78919-13-8, Iloprost
79517-01-4, Octreotide acetate 81147-92-4, Esmolol 81403-80-7,
Alfuzosin 82956-11-4, Nafamostat mesilate 83647-97-6, Spirapril
85441-61-8, Quinapril 86541-75-5, Benazepril 87333-19-5, Ramipril
87679-37-6, Trandolapril 88069-67-4, Pilsicainide 88150-42-9,
Amlodipine 88768-40-5, Cilazapril 89226-50-6, Manidipine 89371-37-9,
Imidapril 93107-08-5, Ciprofloxacin hydrochloride 95635-55-5,
Ranolazine 98048-97-6, Fosinopril 99614-01-4, Ondansetron
hydrochloride 100427-26-7, Lercanidipine 103628-48-4, Sumatriptan
succinate 103775-10-6, Moexipril 104713-75-9, Barnidipine
104993-28-4, Fondaparinux 106133-20-4, Tamsulosin 107133-36-8,
Perindopril erbumine **107724-20-9, Eplerenone**
110101-66-1, Tirilazad 113665-84-2, Clopidogrel 114798-26-4, Losartan
115256-11-6, Dofetilide 116308-55-5, Vatanidipine 120993-53-5,
Desirudin 125926-17-2, Sarpogrelate 128270-60-0, Bivalirudin
133040-01-4, Eprosartan 133107-64-9, Insulin lispro 137862-53-4,
Valsartan 138068-37-8, Lepirudin 138402-11-6, Irbesartan
139481-59-7, Candesartan 139755-83-2, Sildenafil 141505-33-1,
Levosimendan 143653-53-6, Abciximab 144494-65-5, Tirofiban
144701-48-4, Telmisartan 147536-97-8, Bosentan 159138-80-4, Cariporide
159776-70-2, Melagatran 166518-60-1, Avasimibe 167305-00-2,
Omapatrilat 168626-94-6, YM087 171596-29-5, Tadalafil 180384-57-0,
Tezosentan 188627-80-7, Eptifibatide 192939-46-1, H376/95
224785-90-4, Vardenafil 516482-86-3, Sermorelin acetate
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(buccal sprays or capsules contg. cardiovascular or renal drugs)

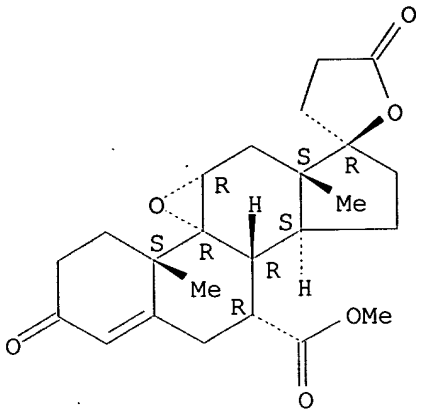
IT **51384-51-1, Metoprolol 107724-20-9, Eplerenone**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(buccal sprays or capsules contg. cardiovascular or renal drugs)

RN 51384-51-1 HCAPLUS
CN 2-Propanol, 1-[4-(2-methoxyethyl)phenoxy]-3-[(1-methylethyl)amino]- (9CI) (CA INDEX NAME)



RN 107724-20-9 HCAPLUS
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, .gamma.-lactone, methyl ester, (7.alpha.,11.alpha.,17.alpha.)- (9CI) (CA INDEX NAME)

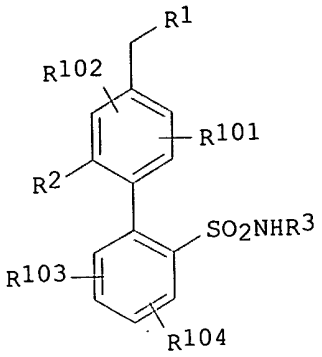
Absolute stereochemistry.



L68 ANSWER 2 OF 4 HCAPLUS COPYRIGHT 2003 ACS
AN 2002:755214 HCAPLUS
DN 137:263024
TI Preparation of N-isoxazolyl biphenylsulfonamides and related compounds as dual angiotensin II and endothelin receptor antagonists.
IN Murugesan, Natesan; Tellew, John E.; Macor, Jhon E.; Gu, Zhengxiang
PA USA
SO U.S. Pat. Appl. Publ., 206 pp., Cont.-in-part of U.S. Ser. No. 643,640, abandoned.
CODEN: USXXCO
DT Patent
LA English
IC ICM A61K031-4166
ICS A61K031-4184; A61K031-4196; C07D233-32; C07D213-68; C07D215-233; C07D249-08
NCL 514258000
CC 28-6 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2002143024	A1	20021003	US 2000-737201	20001214
PRAI	US 1998-91847P	P	19980706		
	US 1999-345392	B2	19990701		
	US 1999-464037	B2	19991215		
	US 2000-481197	B2	20000111		
	US 2000-513779	A2	20000225		
	US 2000-604322	A2	20000626		
	US 2000-643640	B2	20000822		

OS MARPAT 137:263024
GI



I

AB Title compds. (I; R1 = specified oxoimidazolyl, pyridoimidazolyl, pyridylamino, pyridyloxy, triazolyl, quinolinyloxy, etc.; R2 = H, halo, CHO, (halo)alkyl, cycloalkylalkyl, alkenyl, alkynyl, alkoxyalkyl, alkoxy, cyano, OH, NO2, etc.; R3 = heteroaryl; R101-R104 = H, halo, CHO, alkyl, haloalkyl, cycloalkylalkyl, alkenyl, alkynyl, alkoxyalkyl, haloalkoxyalkyl, alkoxy, alkoxyalkoxy, cyano, OH, hydroxyalkyl, NO2, etc; with provisos) were prepd. as dual angiotensin II and endothelin receptor antagonists for treatment of hypertension and other diseases (no data). Thus, 4-BrC6H4CH2OH was coupled with [2-[[(4,5-dimethyl-3-isoxazolyl)[(2-methoxyethoxy)methyl]amino]sulfonyl]phenyl]boronic acid to give N-(4,5-dimethyl-3-isoxazolyl)-4'-(hydroxymethyl)-N-[(2-methoxyethoxy)methyl][1,1'-biphenyl]-2-sulfonamide (66%). This was brominated to give the 4'-bromomethyl deriv. (90%), reacted with 2-butyl-1,3-diazaspiro[4.4]non-1-en-4-one hydrochloride, and deprotected (49% for two steps) to give 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-[1,1'-biphenyl]-2-sulfonamide.

ST isoxazolyl biphenylsulfonamide prepn angiotensin endothelin receptor antagonist; diazaspirononenylmethyldimethylisoxazolylbiphenylsulfonamide prepn angiotensin endothelin receptor antagonist; antihypertensive biphenylsulfonamide prepn

IT Angiotensin receptors
RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)
(angiotensin II, antagonists; prepn. of N-isoxazolyl biphenylsulfonamides and related compds. as dual angiotensin II and endothelin receptor antagonists)

IT Endothelin receptors
RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)
(antagonists; prepn. of N-isoxazolyl biphenylsulfonamides and related compds. as dual angiotensin II and endothelin receptor antagonists)

IT Antiarteriosclerotics
(antiatherosclerotics; prepn. of N-isoxazolyl biphenylsulfonamides and related compds. as dual angiotensin II and endothelin receptor antagonists)

IT Prostate gland, disease
(benign hyperplasia, treatment; prepn. of N-isoxazolyl biphenylsulfonamides and related compds. as dual angiotensin II and endothelin receptor antagonists)

IT Meninges
(disease, subarachnoid hemorrhage, treatment; prepn. of N-isoxazolyl biphenylsulfonamides and related compds. as dual angiotensin II and endothelin receptor antagonists)

IT Sexual behavior
(disorder, treatment of female; prepn. of N-isoxazolyl biphenylsulfonamides and related compds. as dual angiotensin II and

endothelin receptor antagonists)

IT Heart, disease
Kidney, disease
(failure, treatment; prepn. of N-isoxazolyl biphenylsulfonamides and related compds. as dual angiotensin II and endothelin receptor antagonists)

IT Sexual behavior
(impotence, treatment; prepn. of N-isoxazolyl biphenylsulfonamides and related compds. as dual angiotensin II and endothelin receptor antagonists)

IT Antiasthmatics
Antihypertensives
Antimigraine agents
Antitumor agents
Human
(prepn. of N-isoxazolyl biphenylsulfonamides and related compds. as dual angiotensin II and endothelin receptor antagonists)

IT Growth inhibitors, animal
RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of N-isoxazolyl biphenylsulfonamides and related compds. as dual angiotensin II and endothelin receptor antagonists)

IT Artery, disease
(restenosis, treatment; prepn. of N-isoxazolyl biphenylsulfonamides and related compds. as dual angiotensin II and endothelin receptor antagonists)

IT Atherosclerosis
Endotoxemia
Hypertension
Ischemia
(treatment; prepn. of N-isoxazolyl biphenylsulfonamides and related compds. as dual angiotensin II and endothelin receptor antagonists)

IT 62571-86-2, Captopril 74258-86-9, Alacepril 75847-73-3, Enalapril 76547-98-3, Lisinopril 81872-10-8, Zofenopril 82924-03-6, Pentopril 83435-66-9, Delapril 85441-61-8, Quinapril 87333-19-5, Ramipril 98048-97-6, Fosinopril 111223-26-8, Ceranapril 160135-92-2, Gemopatrilat 167305-00-2, Omapatrilat
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(coadministration; prepn. of N-isoxazolyl biphenylsulfonamides and related compds. as dual angiotensin II and endothelin receptor antagonists)

IT 254737-84-3P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)- 254737-85-4P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(3,4-dimethyl-5-isoxazolyl)-2'-[(methylamino)methyl]- 254737-86-5P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(3,4-dimethyl-5-isoxazolyl)-2'-formyl- 254737-87-6P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(3,4-dimethyl-5-isoxazolyl)-2'-[(3,3-dimethyl-2-oxo-1-pyrrolidinyl)methyl]- 254737-88-7P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(3,4-dimethyl-5-isoxazolyl)-2'-[(3-methyl-2-oxo-1-imidazolidinyl)methyl]- 254737-89-8P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[(3,3-dimethyl-2-oxo-1-pyrrolidinyl)methyl]-N-pyrazinyl- 254737-90-1P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(3-chloropyrazinyl)-2'-[(3,3-dimethyl-2-oxo-1-pyrrolidinyl)methyl]- 254737-91-2P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(3,4-dimethyl-5-isoxazolyl)-2'-[(2-oxo-1-pyrrolidinyl)methyl]- 254737-92-3P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[(3,3-

dimethyl-2-oxo-1-pyrrolidinyl)methyl]-N-(3,6-dimethylpyrazinyl)-
254737-94-5P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-
diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[(3,3-dimethyl-2-oxo-1-
pyrrolidinyl)methyl]-N-(3-methoxypyrazinyl)- 254737-96-7P,
[1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-
en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-formyl- 254737-98-9P,
[1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-
en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-[(2-oxo-1-
pyrrolidinyl)methyl]- 254738-00-6P, Pentanamide, N-[[2'-[[(3,4-dimethyl-
5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-N-[(1S)-2-methyl-
1-(3-methyl-1,2,4-oxadiazol-5-yl)propyl]- 254738-03-9P,
[1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-2'-[(3,3-
dimethyl-2-oxo-1-pyrrolidinyl)methyl]-4'-[(2-ethyl-5,7-dimethyl-3H-
imidazo[4,5-b]pyridin-3-yl)methyl]- 254738-05-1P, [1,1'-Biphenyl]-2-
sulfonamide, 4'-[[2-(2-methoxyethyl)-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-
yl]methyl]-N-(3,4-dimethyl-5-isoxazolyl)- 254738-06-2P,
[1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-4'-[[2-
(ethoxymethyl)-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl]methyl]-
254738-07-3P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-
4'-[(2-ethyl-5,7-dimethyl-3H-imidazo[4,5-b]pyridin-3-yl)methyl]-2'-[(2-oxo-
1-pyrrolidinyl)methyl]- 254738-09-5P, [1,1'-Biphenyl]-2-sulfonamide,
N-(3,4-dimethyl-5-isoxazolyl)-4'-[(2-ethyl-5,7-dimethyl-3H-imidazo[4,5-
b]pyridin-3-yl)methyl]-2'-[(3-methyl-2-oxo-1-imidazolidinyl)methyl]-
254738-10-8P, Pentanamide, N-[[2'-[[(3-methyl-5-
isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-N-[(1S)-2-methyl-1-
[(methylamino)carbonyl]propyl]- 254738-11-9P, Pentanamide,
N-[[2'-[[(4-bromo-3-methyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-
yl]methyl]-N-[(1S)-2-methyl-1-[(methylamino)carbonyl]propyl]-
254738-12-0P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-
diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(3,4-dimethyl-5-isoxazolyl)-2'-
propyl- 254738-13-1P, 1H-Benzimidazole-7-carboxylic acid,
1-[[2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-
yl]methyl]-2-ethoxy-, methyl ester 254738-14-2P, 1H-Benzimidazole-7-
carboxylic acid, 1-[[2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-
biphenyl]-4-yl]methyl]-2-ethoxy- 254738-15-3P, 1H-Benzimidazole-7-
carboxylic acid, 1-[[2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-
biphenyl]-4-yl]methyl]-2-ethyl-, methyl ester 254738-16-4P,
1H-Benzimidazole-7-carboxylic acid, 1-[[2'-[[(3,4-dimethyl-5-
isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-2-ethyl-
254738-17-5P, 1H-Benzimidazole-7-carboxylic acid, 1-[[2'-[[(3,4-dimethyl-5-
isoxazolyl)amino]sulfonyl]-2-[(3,3-dimethyl-2-oxo-1-
pyrrolidinyl)methyl][1,1'-biphenyl]-4-yl]methyl]-2-ethoxy-,methylester
254738-18-6P, 1H-Benzimidazole-7-carboxylic acid, 1-[[2'-[[(3,4-dimethyl-5-
isoxazolyl)amino]sulfonyl]-2-[(3,3-dimethyl-2-oxo-1-
pyrrolidinyl)methyl][1,1'-biphenyl]-4-yl]methyl]-2-ethoxy- 254738-19-7P,
1H-Benzimidazole-7-carboxamide, 1-[[2'-[[(3,4-dimethyl-5-
isoxazolyl)amino]sulfonyl]-2-[(3,3-dimethyl-2-oxo-1-
pyrrolidinyl)methyl][1,1'-biphenyl]-4-yl]methyl]-2-ethoxy-N-methyl-
254738-20-0P, 1H-Benzimidazole-7-carboxamide, 1-[[2'-[[(3,4-dimethyl-5-
isoxazolyl)amino]sulfonyl]-2-[(3,3-dimethyl-2-oxo-1-
pyrrolidinyl)methyl][1,1'-biphenyl]-4-yl]methyl]-2-ethoxy-N,N-dimethyl-
254738-21-1P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[[(2-ethyl-4-
quinolinyl)oxy]methyl]-N-(1,3,5-trimethyl-1H-pyrazol-4-yl)- 254738-22-2P
, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(5-acetyl-4-chloro-2-propyl-1H-
imidazol-1-yl)methyl]-N-(3,4-dimethyl-5-isoxazolyl)- 254738-23-3P,
1H-Imidazole-5-carboxylic acid, 4-chloro-1-[[2'-[[(3,4-dimethyl-5-
isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-2-propyl-, methyl
ester 254738-24-4P, 1H-Imidazole-5-carboxamide, 1-[[2'-[[(3,4-dimethyl-5-
isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-4-ethyl-N,N-
dimethyl-2-propyl- 254738-25-5P, [1,1'-Biphenyl]-2-sulfonamide,
4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(3,4-
dimethyl-5-isoxazolyl)-2'-(hydroxymethyl)- 254738-26-6P,
[1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-

en-3-yl)methyl]-N-(3,4-dimethyl-5-isoxazolyl)-2'-(ethoxymethyl)-
254738-27-7P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-
diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(3,4-dimethyl-5-isoxazolyl)-2'-(2-
methoxyethyl)- 254738-28-8P, [1,1'-Biphenyl]-2-sulfonamide,
4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[(3,3-
dimethyl-2-oxo-1-pyrrolidinyl)methyl]-N-(3-methoxy-5-methylpyrazinyl)-
254738-29-9P, [1,1'-Biphenyl]-2-sulfonamide, N-(4-bromo-3-methyl-5-
isoxazolyl)-4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-
[(3,3-dimethyl-2-oxo-1-pyrrolidinyl)methyl]- 254738-30-2P,
[1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-
en-3-yl)methyl]-N-(3,4-dimethyl-5-isoxazolyl)-2'-
[(formylmethylamino)methyl]- 254738-31-3P, Propanamide,
N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(3,4-
dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]methyl]-N-methyl-
254738-32-4P, Cyclopropanecarboxamide, N-[[4-[(2-butyl-4-oxo-1,3-
diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(3,4-dimethyl-5-
isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]methyl]-N-methyl-
254738-33-5P, Propanamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-
en-3-yl)methyl]-2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-
biphenyl]-2-yl]methyl]-N,2-dimethyl- 254738-34-6P, Butanamide,
N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(3,4-
dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]methyl]-N-methyl-
254738-35-7P, Acetamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-
en-3-yl)methyl]-2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-
biphenyl]-2-yl]methyl]-2-methoxy-N-methyl- 254738-36-8P, 4-Pentynamide,
N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(3,4-
dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]methyl]-N-methyl-
254738-37-9P, Cyclobutanecarboxamide, N-[[4-[(2-butyl-4-oxo-1,3-
diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(3,4-dimethyl-5-
isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]methyl]-N-methyl-
254738-38-0P, Butanamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-
en-3-yl)methyl]-2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-
biphenyl]-2-yl]methyl]-N,3-dimethyl- 254738-39-1P, Propanamide,
N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(3,4-
dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]methyl]-N,2,2-
trimethyl- 254738-40-4P, Propanamide, N-[[4-[(2-butyl-4-oxo-1,3-
diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(3,4-dimethyl-5-
isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]methyl]-3-methoxy-N-methyl-
254738-41-5P, Acetamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-
3-yl)methyl]-2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-
biphenyl]-2-yl]methyl]-2-ethoxy-N-methyl- 254738-42-6P,
2-Furancarboxamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-
yl)methyl]-2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-
2-yl]methyl]-N-methyl- 254738-43-7P, Pentanamide, N-[[4-[(2-butyl-4-oxo-
1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(3,4-dimethyl-5-
isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]methyl]-N,4-dimethyl-
254738-44-8P, Benzamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-
3-yl)methyl]-2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-
biphenyl]-2-yl]methyl]-N-methyl- 254738-45-9P, 3-Thiophenecarboxamide,
N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(3,4-
dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]methyl]-N-methyl-
254738-46-0P, Cyclopentaneacetamide, N-[[4-[(2-butyl-4-oxo-1,3-
diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(3,4-dimethyl-5-
isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]methyl]-N-methyl-
254738-47-1P, Cyclohexanecarboxamide, N-[[4-[(2-butyl-4-oxo-1,3-
diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(3,4-dimethyl-5-
isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]methyl]-N-methyl-
254738-48-2P, Benzamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-
3-yl)methyl]-2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-
biphenyl]-2-yl]methyl]-N,3-dimethyl- 254738-49-3P, Benzeneacetamide,
N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(3,4-
dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]methyl]-N-methyl-
254738-50-6P, Benzamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-

en-3-yl)methyl]-2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]methyl]-2-fluoro-N-methyl- 254738-51-7P, Benzamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]methyl]-3-fluoro-N-methyl- 254738-52-8P, Benzamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]methyl]-4-fluoro-N-methyl- 254738-53-9P, Cyclohexaneacetamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]methyl]-N-methyl- 254738-54-0P, Benzeneacetamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]methyl]-2-fluoro-N-methyl- 254738-55-1P, Benzeneacetamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]methyl]-3-fluoro-N-methyl- 254738-56-2P, Benzeneacetamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]methyl]-4-fluoro-N-methyl- 254738-57-3P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[[(dimethylamino)carbonyl]methylamino]methyl]-N-(3,4-dimethyl-5-isoxazolyl)- 254738-58-4P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[[[(1,1-dimethylethyl)amino]carbonyl]methylamino]methyl]-N-(3,4-dimethyl-5-isoxazolyl)- 254738-59-5P, Carbamic acid, [[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]methyl]methyl-, ethyl ester 254738-60-8P, Carbamic acid, [[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]methyl]methyl-, 2-methylpropyl ester 254738-61-9P, Butanamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]methyl]-N,3,3-trimethyl- 254738-62-0P, 2-Pyridinecarboxamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]methyl]-N-methyl- 254738-63-1P, 3-Pyridinecarboxamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]methyl]-N-methyl- 254738-64-2P, Pyrazinecarboxamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]methyl]-N-methyl- 254738-65-3P, 1H-Pyrrole-2-carboxamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]methyl]-N,1-dimethyl- 254738-66-4P, 1,2,3-Thiadiazole-4-carboxamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]methyl]-N-methyl- 254738-67-5P, Pyrazinecarboxamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]methyl]-N,5-dimethyl- 254738-68-6P, 4-Isoxazolecarboxamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]methyl]-N,3,5-trimethyl- 254738-69-7P, 2-Thiophenecarboxamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]methyl]-N,3-dimethyl- 254738-70-0P, 2-Thiophenecarboxamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]methyl]-N,5-dimethyl- 254738-71-1P, Benzamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]methyl]-3-cyano-N-methyl- 254738-72-2P, Benzamide,

N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]methyl]-4-cyano-N-methyl- 254738-73-3P, Benzamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]methyl]-2-methoxy-N-methyl- 254738-74-4P, Benzamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]methyl]-2-chloro-N-methyl- 254738-75-5P, Benzamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]methyl]-3-chloro-N-methyl- 254738-76-6P, Benzamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]methyl]-4-chloro-N-methyl- 254738-78-8P, Benzamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]methyl]-2,3-difluoro-N-methyl- 254738-79-9P, Benzamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]methyl]-3,4-difluoro-N-methyl- 254738-80-2P, Benzamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]methyl]-3,5-difluoro-N-methyl- 254738-81-3P, Benzamide, 4-acetyl-N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]methyl]-N-methyl- 254738-82-4P, 2-Thiophenecarboxamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]methyl]-3-ethoxy-N-methyl- 254738-83-5P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(3,4-dimethyl-5-isoxazolyl)- 254738-84-6P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(3,4-dimethyl-5-isoxazolyl)-2'-[(propylsulfonyl)amino]- 254738-85-7P, L-Valine, N-[[2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-N-(1-oxopentyl)-, methyl ester 254738-86-8P, L-Valine, N-[[2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-N-(1-oxopentyl)- 254738-87-9P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-2'-[(3,3-dimethyl-2-oxo-1-pyrrolidinyl)methyl]-4'-[(4-oxo-2-propyl-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]- 254738-88-0P, Butanamide, N-[[2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl]-4-[(2-ethyl-5,7-dimethyl-3H-imidazo[4,5-b]pyridin-3-yl)methyl][1,1'-biphenyl]-2-yl]methyl]-N,3,3-trimethyl- 254738-89-1P, Pentanamide, N-[(1S)-1-(aminocarbonyl)-2-methylpropyl]-N-[[2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]- 254738-90-4P, Pentanamide, N-[[2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-N-[(1S)-2-methyl-1-[(methylamino)carbonyl]propyl]- 254738-91-5P, Pentanamide, N-[(1S)-1-[(dimethylamino)carbonyl]-2-methylpropyl]-N-[[2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]- 254738-92-6P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(3,4-dimethyl-5-isoxazolyl)-2'-[[(2,2,2-trifluoroethyl)amino]methyl]- 254738-93-7P, [1,1'-Biphenyl]-2-carboxylic acid, 4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl]- 254738-94-8P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(3,4-dimethyl-5-isoxazolyl)-2'-(trifluoromethyl)- 254738-95-9P, [1,1'-Biphenyl]-2-carboxylic acid, 4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl]-, methyl ester 254738-96-0P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(3,4-dimethyl-5-isoxazolyl)-2'-(methoxymethyl)- 254738-97-1P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(3,4-dimethyl-5-isoxazolyl)-2'-fluoro- 254738-98-2P, [1,1'-Biphenyl]-2-sulfonamide, 2'-(cyanomethyl)-N-(3,4-dimethyl-5-isoxazolyl)-4'-[(2-ethyl-5,7-dimethyl-

3H-imidazo[4,5-b]pyridin-3-yl)methyl]- 254738-99-3P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-(cyanomethyl)-N-(3,4-dimethyl-5-isoxazolyl)- 254739-00-9P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-cyano-N-(3,4-dimethyl-5-isoxazolyl)- 254739-01-0P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(3,4-dimethyl-5-isoxazolyl)-2'-methyl- 254739-02-1P, [1,1'-Biphenyl]-2-sulfonamide, 2'-cyano-N-(3,4-dimethyl-5-isoxazolyl)-4'-[(2-ethyl-5,7-dimethyl-3H-imidazo[4,5-b]pyridin-3-yl)methyl]- 254739-03-2P, Pentanamide, N-[[2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl]-2-methyl[1,1'-biphenyl]-4-yl]methyl]-N-[(1S)-2-methyl-1-[(methylamino)carbonyl]propyl]- 254739-04-3P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-4'-[(2-ethyl-5,7-dimethyl-3H-imidazo[4,5-b]pyridin-3-yl)methyl]-2'-[[(2,2,2-trifluoroethyl)amino]methyl]- 254739-05-4P, Benzeneacetamide, N-[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]- 254739-06-5P, Butanamide, N-[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]-3,3-dimethyl- 254739-07-6P, [1,1'-Biphenyl]-2-sulfonamide, 2'-amino-4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(3,4-dimethyl-5-isoxazolyl)- 254739-08-7P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(3,4-dimethyl-5-isoxazolyl)-2'-nitro- 254739-09-8P, Pentanamide, 2-[[[2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl](1-oxopropyl)amino]-N,3-dimethyl-, (2S,3S)- 254739-10-1P, Cyclopropanecarboxamide, N-[[2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-N-[(1S,2S)-2-methyl-1-[(methylamino)carbonyl]butyl]- 254739-11-2P, Benzenepropanamide, N-[[2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-N-[(1S,2S)-2-methyl-1-[(methylamino)carbonyl]butyl]- 254739-12-3P, Pentanamide, 2-[[[2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl](3-methyl-1-oxobutyl)amino]-N,3-dimethyl-, (2S,3S)- 254739-13-4P, Hexanamide, N-[[2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-N-[(1S,2S)-2-methyl-1-[(methylamino)carbonyl]butyl]- 254739-14-5P, Pentanamide, 2-[[[2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl](1-oxobutyl)amino]-N,3-dimethyl-, (2S,3S)- 254739-15-6P, Pentanamide, 2-[[[2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl](1-oxopropyl)amino]-N,4-dimethyl-, (2S)- 254739-16-7P, Cyclopropanecarboxamide, N-[[2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-N-[(1S)-3-methyl-1-[(methylamino)carbonyl]butyl]- 254739-17-8P, Benzenepropanamide, N-[[2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-N-[(1S)-3-methyl-1-[(methylamino)carbonyl]butyl]- 254739-18-9P, Benzeneacetamide, N-[[2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-N-[(1S)-3-methyl-1-[(methylamino)carbonyl]butyl]- 254739-19-0P, Pentanamide, 2-[[[2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl](3-methyl-1-oxobutyl)amino]-N,4-dimethyl-, (2S)- 254739-20-3P, Hexanamide, N-[[2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-N-[(1S)-3-methyl-1-[(methylamino)carbonyl]butyl]- 254739-21-4P, Pentanamide, 2-[[[2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl](1-oxobutyl)amino]-N,4-dimethyl-, (2S)- 254739-22-5P, Butanamide, 2-[[[2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl](1-oxopropyl)amino]-N,3-dimethyl-, (2S)- 254739-23-6P, Cyclopropanecarboxamide, N-[[2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-N-[(1S)-2-methyl-1-[(methylamino)carbonyl]propyl]- 254739-24-7P, Benzenepropanamide, N-[[2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-N-[(1S)-2-methyl-1-

[(methylamino)carbonyl]propyl]- 254739-25-8P, Benzeneacetamide, N-[[2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-N-[(1S)-2-methyl-1-[(methylamino)carbonyl]propyl]- 254739-26-9P, Butanamide, 2-[[[2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl](3-methyl-1-oxobutyl)amino]-N,3-dimethyl-, (2S)- 254739-27-0P, Hexanamide, N-[[2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-N-[(1S)-2-methyl-1-[(methylamino)carbonyl]propyl]- 254739-28-1P, Butanamide, 2-[[[2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl](1-oxobutyl)amino]-N,3-dimethyl-, (2S)- 254739-29-2P, Pentanamide, N-[[2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-N-[(1S)-1-[(ethylamino)carbonyl]-2-methylpropyl]- 254739-30-5P, Pentanamide, N-[[2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-N-[(1S)-1-[(hexylamino)carbonyl]-2-methylpropyl]- 254739-31-6P, Pentanamide, N-[[2-cyano-2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-N-[(1S)-2-methyl-1-[(methylamino)carbonyl]propyl]- 254739-32-7P, Pentanamide, N-[[2-(cyanomethyl)-2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-N-[(1S)-2-methyl-1-[(methylamino)carbonyl]propyl]- 254739-33-8P, [1,1'-Biphenyl]-2-carboxamide, 4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl]- 254739-34-9P, [1,1'-Biphenyl]-2-carboxamide, 4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl]-N,N-dimethyl- 254739-35-0P, [1,1'-Biphenyl]-2-carboxamide, 4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl]-N-methyl- 254739-36-1P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-2'-(methoxymethyl)-4'-[(5,6,7,8-tetrahydro-8-oxo-2-propyl-1(4H)-cycloheptimidazolyl)methyl]- 254739-37-2P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-4'-[[(3-methoxy-2,6-dimethyl-4-pyridinyl)oxy]methyl]-2'-methyl- 254739-38-3P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-2'-methyl-4'-[(5,6,7,8-tetrahydro-8-oxo-2-propyl-1(4H)-cycloheptimidazolyl)methyl]- 254739-39-4P, Butanamide, 2-[[[2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl]-2-(methoxymethyl)[1,1'-biphenyl]-4-yl]methyl](1-oxobutyl)amino]-N,3-dimethyl-, (2S)- 254739-40-7P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-2'-(hydroxymethyl)-4'-[(5,6,7,8-tetrahydro-8-oxo-2-propyl-1(4H)-cycloheptimidazolyl)methyl]- 254739-41-8P, [1,1'-Biphenyl]-2-sulfonamide, 2'-chloro-N-(3,4-dimethyl-5-isoxazolyl)-4'-[[(2-ethyl-5,6,7,8-tetrahydro-4-quinolinyl)oxy]methyl]- 254739-42-9P, Butanamide, 2-[[[2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl]-2-fluoro[1,1'-biphenyl]-4-yl]methyl](1-oxobutyl)amino]-N,3-dimethyl-, (2S)- 254739-43-0P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(3,4-dimethyl-5-isoxazolyl)-2'-(phenoxymethyl)- 254739-44-1P, Butanamide, 2-[[[2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl]-2-(1H-pyrazol-1-ylmethyl)[1,1'-biphenyl]-4-yl]methyl](1-oxobutyl)amino]-N,3-dimethyl-, (2S)- 254739-45-2P, Cyclopropanecarboxamide, N-[(1S)-1-[(dimethylamino)carbonyl]-2-methylpropyl]-N-[[2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]- 254739-46-3P, Butanamide, 2-[[[2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl](1-oxobutyl)amino]-N,N,3-trimethyl-, (2S)- 254739-47-4P, Cyclopropanecarboxamide, N-[(1S)-1-[(dimethylamino)carbonyl]-2-methylpropyl]-N-[[2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl]-2-(methoxymethyl)[1,1'-biphenyl]-4-yl]methyl]- 254739-48-5P, Butanamide, 2-[[[2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl]-2-(methoxymethyl)[1,1'-biphenyl]-4-yl]methyl](1-oxobutyl)amino]-N,N,3-trimethyl-, (2S) 254739-49-6P, Pentanamide, N-[[2-chloro-2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-N-[(1S)-2-methyl-1-[(methylamino)carbonyl]propyl]- 254739-50-9P, Pentanamide, N-[[2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl]-2-(trifluoromethyl)[1,1'-biphenyl]-4-yl]methyl]-N-[(1S)-2-methyl-1-

[(methylamino)carbonyl]propyl]- 254739-51-0P, Cyclobutanecarboxamide, N-[[2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-N-[(1S)-2-methyl-1-[(methylamino)carbonyl]propyl]- 254739-52-1P, 1H-Imidazole-5-carboxylic acid, 1-[[2-chloro-2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-4-ethyl-2-propyl- 254739-53-2P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(3,4-dimethyl-5-isoxazolyl)-2'-[(methylsulfonyl)amino]- 254739-54-3P, Pentanamide, N-[[2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-N-[(1S)-2-methyl-1-[(4-methyl-1-piperazinyl)carbonyl]propyl]- 254739-55-4P, Pentanamide, N-[[2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-N-[(1S)-2-methyl-1-(1-piperidinylcarbonyl)propyl]- 254739-56-5P, Pentanamide, N-[(1S)-1-[[(3,3-dimethylbutyl)amino]carbonyl]-2-methylpropyl]-N-[[2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]- 254739-57-6P, Pentanamide, N-[[2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-N-[(1S)-1-[[[(4-fluorophenyl)methyl]amino]carbonyl]-2-methylpropyl]- 254739-58-7P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(3,4-dimethyl-5-isoxazolyl)-2'-[(1-methylethoxy)methyl]-

RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of N-isoxazolyl biphenylsulfonamides and related compds. as dual angiotensin II and endothelin receptor antagonists)

IT 254739-59-8P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(3,4-dimethyl-5-isoxazolyl)-2'-(propoxymethyl)- 254739-60-1P, 1H-Imidazole-5-carboxamide, 4-chloro-1-[[2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-2-propyl- 254739-61-2P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-2'-fluoro-4'-[(5,6,7,8-tetrahydro-8-oxo-2-propyl-1(4H)-cycloheptimidazolyl)methyl]- 254739-62-3P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(3,4-dimethyl-5-isoxazolyl)-2'-[(2-oxo-1(2H)-pyridinyl)methyl]- 254739-63-4P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(3,4-dimethyl-5-isoxazolyl)-2'-(1H-pyrazol-1-ylmethyl)- 254739-64-5P, 1H-Imidazole-5-carboxamide, 2-butyl-4-chloro-1-[[2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]- 254739-65-6P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-4'-[[(2-methyl-4-quinolinyl)oxy]methyl]- 254739-66-7P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-4'-[[(2-ethyl-4-quinolinyl)oxy]methyl]- 254739-67-8P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-4'-[[(2-ethyl-5,6,7,8-tetrahydro-4-quinolinyl)oxy]methyl]- 254739-68-9P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-4'-[[(2-propyl-4-quinolinyl)oxy]methyl]- 254739-69-0P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(6,7-dihydro-2,4-dimethyl-7-oxopyrido[2,3-d]pyrimidin-8(5H)-yl)methyl]-N-(3,4-dimethyl-5-isoxazolyl)- 254739-70-3P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-2'-[(3,3-dimethyl-2-oxo-1-pyrrolidinyl)methyl]-4'-[[(2-ethyl-4-quinolinyl)oxy]methyl]- 254739-71-4P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-2'-[(3,3-dimethyl-2-oxo-1-pyrrolidinyl)methyl]-4'-[[(2-ethyl-5,6,7,8-tetrahydro-4-quinolinyl)oxy]methyl]- 254739-72-5P, 1H-Benzimidazole-7-carboxamide, 1-[[2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-2-ethyl-N-methyl- 254739-73-6P, 1H-Benzimidazole-7-carboxylic acid, 1-[[2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-2-ethyl-, phenylmethyl ester 254739-74-7P, 1H-Benzimidazole-7-carboxylic acid, 1-[[2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-2-ethyl-, 2-phenylethyl ester 254739-75-8P, 1H-Benzimidazole-7-carboxylic acid, 1-[[2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-

yl]methyl]-2-ethyl-, 2-(2-oxo-1-pyrrolidinyl)ethyl ester 254739-76-9P, 1H-Benzimidazole-7-carboxylic acid, 1-[[2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-2-ethyl-, 3-(2-oxo-1-pyrrolidinyl)propyl ester 254739-77-0P, [1,1'-Biphenyl]-2-sulfonamide, 2'-cyano-N-(3,4-dimethyl-5-isoxazolyl)-4'-[[(2-ethyl-4-quinolinyl)oxy]methyl]- 254739-79-2P, [1,1'-Biphenyl]-2-sulfonamide, 2'-(cyanomethyl)-N-(3,4-dimethyl-5-isoxazolyl)-4'-[(5,6,7,8-tetrahydro-8-oxo-2-propyl-1(4H)-cycloheptimidazolyl)methyl]- 254739-80-5P, 1H-Imidazole-5-carboxamide, 1-[[2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-4-ethyl-N-methyl-2-propyl- 254739-81-6P, 1H-Imidazole-5-carboxamide, 1-[[2-chloro-2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-4-ethyl-2-propyl- 254739-82-7P, 1H-Imidazole-5-carboxamide, 1-[[2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-4-ethyl-2-propyl- 254739-83-8P, 1H-Benzimidazole-7-carboxamide, 1-[[2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-2-ethoxy-N-methyl- 254739-84-9P, 1H-Benzimidazole-7-carboxamide, 1-[[2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-2-ethoxy-N,N-dimethyl- 254739-85-0P, 3-Pyridinecarboxylic acid, 2-[[[2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]propylamino]- 254739-86-1P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(3,5-dibutyl-1H-1,2,4-triazol-1-yl)methyl]-N-(3,4-dimethyl-5-isoxazolyl)- 254739-87-2P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-4'-[(5,6,7,8-tetrahydro-8-oxo-2-propyl-1(4H)-cycloheptimidazolyl)methyl]- 254739-88-3P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2,7-diethyl-5H-pyrazolo[1,5-b][1,2,4]triazol-5-yl)methyl]-N-(3,4-dimethyl-5-isoxazolyl)- 254739-89-4P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[[2-butyl-6-[[[methyl(1-methylethyl)amino]carbonyl]amino]-4-oxo-3(4H)-quinazolinyl]methyl]-N-(3,4-dimethyl-5-isoxazolyl)- 254739-90-7P, 3-Pyridinecarboxamide, 2-[[[2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]propylamino]-N-methyl- 254739-91-8P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-4'-[[(3-methoxy-2,6-dimethyl-4-pyridinyl)oxy]methyl]- 254739-92-9P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-2'-[(3,3-dimethyl-2-oxo-1-pyrrolidinyl)methyl]-4'-[[(3-methoxy-2,6-dimethyl-4-pyridinyl)oxy]methyl]- 254739-93-0P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-2'-[(3,3-dimethyl-2-oxo-1-pyrrolidinyl)methyl]-4'-[(5,6,7,8-tetrahydro-8-oxo-2-propyl-1(4H)-cycloheptimidazolyl)methyl]- 254739-94-1P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-4'-[[(3-methoxy-2,6-dimethyl-4-pyridinyl)oxy]methyl]-2'-(methoxymethyl)- 254739-95-2P, 1H-Imidazole-5-carboxamide, 1-[[2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-2-ethyl-4-methyl- 254739-96-3P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-3(4H)-quinazolinyl)methyl]-N-(3,4-dimethyl-5-isoxazolyl)- 254739-97-4P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-[(3,3-dimethyl-2-oxo-1-pyrrolidinyl)methyl]- 254739-98-5P, Pentanamide, N-[[2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl]-2-[(3,3-dimethyl-2-oxo-1-pyrrolidinyl)methyl][1,1'-biphenyl]-4-yl]methyl]-N-[(1S)-2-methyl-1-[(methylamino)carbonyl]propyl]- 254739-99-6P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(3,4-dimethyl-5-isoxazolyl)-2'-[(4,4-dimethyl-2-oxo-1-pyrrolidinyl)methyl]- 254740-00-6P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(3,5-dibutyl-1H-1,2,4-triazol-1-yl)methyl]-N-(3,4-dimethyl-5-isoxazolyl)-2'-[(3,3-dimethyl-2-oxo-1-pyrrolidinyl)methyl]- 254740-01-7P, Acetamide, N-[2-[[[2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl]-4-[(2-ethyl-5,7-dimethyl-3H-imidazo[4,5-b]pyridin-3-yl)methyl][1,1'-biphenyl]-2-yl]methyl]methylamino]ethyl]- 254740-02-8P, [1,1'-Biphenyl]-2-acetic acid, 2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl]-4-[(2-ethyl-5,7-dimethyl-3H-imidazo[4,5-b]pyridin-3-yl)methyl]-, ethyl ester 254740-03-9P, Pentanamide, N-[[2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-

yl]methyl]-N-[(1S)-2-methyl-1-[(propylamino)carbonyl]propyl]-
254740-04-0P, Pentanamide, N-[[2'-[[(3,4-dimethyl-5-
isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-N-[(1S)-2-methyl-1-
[[[(tetrahydro-2-furanyl)methyl]amino]carbonyl]propyl]- 254740-05-1P,
[1,1'-Biphenyl]-2-sulfonamide, 2'-chloro-N-(3,4-dimethyl-5-isoxazolyl)-4'-
[[(2-ethyl-4-quinolinyl)oxy]methyl]- 254740-06-2P, [1,1'-Biphenyl]-2-
sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-4'-[[(2-ethyl-4-
quinolinyl)oxy]methyl]-2'-(trifluoromethyl)- 254740-07-3P,
[1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-
en-3-yl)methyl]-2'-chloro-N-(3,4-dimethyl-5-isoxazolyl)- 254740-08-4P,
[1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-
en-3-yl)methyl]-N-(3,4-dimethyl-5-isoxazolyl)-2'-[(2-methylpropoxy)methyl]-
254740-09-5P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-
diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(3,4-dimethyl-5-isoxazolyl)-2'-
[(ethylsulfonyl)amino]- 254740-10-8P, [1,1'-Biphenyl]-2-sulfonamide,
4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(3,4-
dimethyl-5-isoxazolyl)-2'-[(2,2,2-trifluoroethoxy)methyl]- 254740-11-9P,
[1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-
en-3-yl)methyl]-N-(3,4-dimethyl-5-isoxazolyl)-2'-[(2-fluoroethoxy)methyl]-
254740-12-0P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-
2'-(ethoxymethyl)-4'-[[(3-methoxy-2,6-dimethyl-4-pyridinyl)oxy]methyl]-
254740-15-3P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-
2'-(ethoxymethyl)-4'-[(5,6,7,8-tetrahydro-8-oxo-2-propyl-1(4H)-
cycloheptimidazolyl)methyl]- 254740-18-6P, [1,1'-Biphenyl]-2-
sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-
(3,4-dimethyl-5-isoxazolyl)-2'-(3,3,3-trifluoropropyl)- 254740-20-0P,
[1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-
en-3-yl)methyl]-N-(3,4-dimethyl-5-isoxazolyl)-2'-(3-fluoropropyl)-
254740-21-1P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-
diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-(1,1-difluoroethyl)-N-(3,4-
dimethyl-5-isoxazolyl)- 254740-22-2P, [1,1'-Biphenyl]-2-sulfonamide,
4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(3,4-
dimethyl-5-isoxazolyl)-2'-(2,2,2-trifluoroethyl)- 254740-23-3P,
[1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-
en-3-yl)methyl]-N-(3,4-dimethyl-5-isoxazolyl)-2'-(2-methylpropoxy)-
254740-24-4P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-
diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(3,4-dimethyl-5-isoxazolyl)-2'-(2-
methoxyethoxy)- 254740-25-5P, [1,1'-Biphenyl]-2-sulfonamide,
2'-butyl-4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-
(3,4-dimethyl-5-isoxazolyl)- 254740-26-6P, [1,1'-Biphenyl]-2-
sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-
(3-methyl-5-isoxazolyl)-2'-(trifluoromethyl)- 254740-27-7P,
[1,1'-Biphenyl]-2-sulfonamide, N-(4-bromo-3-methyl-5-isoxazolyl)-4'-[(2-
butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-(trifluoromethyl)-
254740-28-8P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-
diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4-chloro-3-methyl-5-isoxazolyl)-2'-
(trifluoromethyl)- 254740-29-9P, [1,1'-Biphenyl]-2-sulfonamide,
4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(3,4-
dimethyl-5-isoxazolyl)-2'-[(methoxymethylamino)methyl]- 254740-30-2P,
[1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-
en-3-yl)methyl]-2'-[(2,2-difluoroethoxy)methyl]-N-(3,4-dimethyl-5-
isoxazolyl)- 254740-31-3P, [1,1'-Biphenyl]-2-sulfonamide,
4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(3,4-
dimethyl-5-isoxazolyl)-2'-(2-fluoroethyl)- 254740-32-4P,
[1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-
en-3-yl)methyl]-N-(3,4-dimethyl-5-isoxazolyl)-2'-(2-hydroxyethyl)-
254740-33-5P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-
diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(3,4-dimethyl-5-isoxazolyl)-2'-(3-
methylbutyl)- 254740-34-6P, [1,1'-Biphenyl]-2-sulfonamide,
4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(3,4-
dimethyl-5-isoxazolyl)-2'-(2-methylpropyl)- 254740-35-7P,
[1,1'-Biphenyl]-2-sulfonamide, 4'-[[2-(3,3-difluorobutyl)-4-oxo-1,3-
diazaspiro[4.4]non-1-en-3-yl]methyl]-N-(3,4-dimethyl-5-isoxazolyl)-2'-

(ethoxymethyl)- 254740-36-8P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-4'-[[(3-methoxy-2,6-dimethyl-4-pyridinyl)oxy]methyl]-2'-(3,3,3-trifluoropropyl)- 254740-37-9P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[(1,1-dimethylethoxy)methyl]-N-(3,4-dimethyl-5-isoxazolyl)- 254740-38-0P, 1H-Imidazole-5-carboxamide, 1-[[2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl]-2-(methoxymethyl)[1,1'-biphenyl]-4-yl]methyl]-4-ethyl-2-propyl- 254740-39-1P, 1H-Imidazole-5-carboxamide, 1-[[2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl]-2-(methoxymethyl)[1,1'-biphenyl]-4-yl]methyl]-4-ethyl-N-methyl-2-propyl- 254740-40-4P, 1H-Imidazole-5-carboxamide, 1-[[2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl]-2-methyl[1,1'-biphenyl]-4-yl]methyl]-4-ethyl-2-propyl- 254740-41-5P, 1H-Imidazole-5-carboxamide, 1-[[2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl]-2-methyl[1,1'-biphenyl]-4-yl]methyl]-4-ethyl-N-methyl-2-propyl- 254740-42-6P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-[(methylamino)methyl]- 254740-43-7P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-[(3-methyl-2-oxo-1-imidazolidinyl)methyl]- 254740-44-8P, Pentanamide, N-[[2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-N-[(1S)-2-methyl-1-(3-methyl-1,2,4-oxadiazol-5-yl)propyl]- 254740-45-9P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-2'-[(3,3-dimethyl-2-oxo-1-pyrrolidinyl)methyl]-4'-[(2-ethyl-5,7-dimethyl-3H-imidazo[4,5-b]pyridin-3-yl)methyl]- 254740-46-0P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-4'-[[2-(2-methoxyethyl)-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl]methyl]- 254740-47-1P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-4'-[[2-(ethoxymethyl)-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl]methyl]- 254740-48-2P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-4'-[(2-ethyl-5,7-dimethyl-3H-imidazo[4,5-b]pyridin-3-yl)methyl]-2'-[(2-oxo-1-pyrrolidinyl)methyl]- 254740-49-3P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-4'-[(2-ethyl-5,7-dimethyl-3H-imidazo[4,5-b]pyridin-3-yl)methyl]-2'-[(3-methyl-2-oxo-1-imidazolidinyl)methyl]- 254740-50-6P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-propyl- 254740-51-7P, 1H-Benzimidazole-7-carboxylic acid, 1-[[2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-2-ethoxy-, methyl ester 254740-52-8P, 1H-Benzimidazole-7-carboxylic acid, 1-[[2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-2-ethoxy- 254740-53-9P, 1H-Benzimidazole-7-carboxylic acid, 1-[[2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-2-ethyl-, methyl ester 254740-54-0P, 1H-Benzimidazole-7-carboxylic acid, 1-[[2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-2-ethyl- 254740-55-1P, 1H-Benzimidazole-7-carboxylic acid, 1-[[2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl]-2-[(3,3-dimethyl-2-oxo-1-pyrrolidinyl)methyl][1,1'-biphenyl]-4-yl]methyl]-2-ethoxy-,methylester 254740-56-2P, 1H-Benzimidazole-7-carboxylic acid, 1-[[2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl]-2-[(3,3-dimethyl-2-oxo-1-pyrrolidinyl)methyl][1,1'-biphenyl]-4-yl]methyl]-2-ethoxy- 254740-57-3P, 1H-Benzimidazole-7-carboxamide, 1-[[2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl]-2-[(3,3-dimethyl-2-oxo-1-pyrrolidinyl)methyl][1,1'-biphenyl]-4-yl]methyl]-2-ethoxy-N-methyl- 254740-58-4P, 1H-Benzimidazole-7-carboxamide, 1-[[2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl]-2-[(3,3-dimethyl-2-oxo-1-pyrrolidinyl)methyl][1,1'-biphenyl]-4-yl]methyl]-2-ethoxy-N,N-dimethyl- 254740-59-5P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[[(2-ethyl-4-quinolinyl)oxy]methyl]-N-(3-methyl-5-isoxazolyl)- 254740-60-8P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(5-acetyl-4-chloro-2-propyl-1H-imidazol-1-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)- 254740-61-9P, 1H-Imidazole-5-carboxylic acid, 4-chloro-1-[[2'-[[(4,5-dimethyl-3-

isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-2-propyl-, methyl ester 254740-62-0P, 1H-Imidazole-5-carboxamide, 1-[[2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-4-ethyl-N,N-dimethyl-2-propyl- 254740-63-1P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-(hydroxymethyl)- 254740-64-2P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-(ethoxymethyl)- 254740-65-3P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-(2-methoxyethyl)- 254740-66-4P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-[(formylmethylamino)methyl]- 254740-67-5P, Propanamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]methyl]-N-methyl- 254740-68-6P, Cyclopropanecarboxamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]methyl]-N-methyl- 254740-69-7P, Propanamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]methyl]-N,2-dimethyl- 254740-70-0P, Butanamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]methyl]-N-methyl- 254740-71-1P, Acetamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]methyl]-2-methoxy-N-methyl- 254740-72-2P, 4-Pentynamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]methyl]-N-methyl- 254740-73-3P, Cyclobutanecarboxamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]methyl]-N-methyl- 254740-74-4P, Butanamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]methyl]-N,3-dimethyl- 254740-75-5P, Propanamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]methyl]-N,2,2-trimethyl- 254740-76-6P, Propanamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]methyl]-3-methoxy-N-methyl- 254740-77-7P, Acetamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]methyl]-2-ethoxy-N-methyl- 254740-78-8P, 2-Furancarboxamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]methyl]-N-methyl- 254740-79-9P, Pentanamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]methyl]-N,4-dimethyl- 254740-80-2P, Benzamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]methyl]-N-methyl- 254740-81-3P, 3-Thiophenecarboxamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]methyl]-N-methyl- 254740-82-4P, Cyclopentaneacetamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]methyl]-N-methyl- 254740-83-5P, Cyclohexanecarboxamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]methyl]-N-methyl- 254740-84-6P, Benzamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]methyl]-N,3-dimethyl- 254740-85-7P, Benzeneacetamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]methyl]-N-methyl-

254740-86-8P, Benzamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]methyl]-2-fluoro-N-methyl- 254740-87-9P, Benzamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]methyl]-3-fluoro-N-methyl- 254740-88-0P, Benzamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]methyl]-4-fluoro-N-methyl- 254740-89-1P, Cyclohexaneacetamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]methyl]-N-methyl- 254740-90-4P, Benzeneacetamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]methyl]-2-fluoro-N-methyl- 254740-91-5P

, Benzeneacetamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]methyl]-3-fluoro-N-methyl- 254740-92-6P, Benzeneacetamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]methyl]-4-fluoro-N-methyl- 254740-93-7P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[[(dimethylamino)carbonyl]methylamino]methyl]-N-(4,5-dimethyl-3-isoxazolyl)- 254740-94-8P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[[[(1,1-dimethylethyl)amino]carbonyl]methylamino]methyl]-N-(4,5-dimethyl-3-isoxazolyl)- 254740-95-9P, Carbamic acid, [[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]methyl]methyl-, ethyl ester 254740-96-0P, Carbamic acid, [[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]methyl]methyl-, 2-methylpropyl ester 254740-97-1P, Butanamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]methyl]-N,3,3-trimethyl- 254740-98-2P, 2-Pyridinecarboxamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]methyl]-N-methyl- 254740-99-3P, 3-Pyridinecarboxamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]methyl]-N-methyl- 254741-00-9P, Pyrazinecarboxamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]methyl]-N-methyl- 254741-01-0P, 1H-Pyrrole-2-carboxamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]methyl]-N,1-dimethyl- 254741-02-1P, 1,2,3-Thiadiazole-4-carboxamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]methyl]-N-methyl- 254741-03-2P, Pyrazinecarboxamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]methyl]-N,5-dimethyl- 254741-04-3P, 4-Isoxazolecarboxamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]methyl]-N,3,5-trimethyl- 254741-05-4P, 2-Thiophenecarboxamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]methyl]-N,3-dimethyl- 254741-06-5P, 2-Thiophenecarboxamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]methyl]-N,5-dimethyl- 254741-07-6P, Benzamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-

biphenyl]-2-yl]methyl]-3-cyano-N-methyl- 254741-08-7P, Benzamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]methyl]-4-cyano-N-methyl- 254741-09-8P, Benzamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]methyl]-2-methoxy-N-methyl- 254741-10-1P, Benzamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]methyl]-2-chloro-N-methyl- 254741-11-2P, Benzamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]methyl]-3-chloro-N-methyl- 254741-12-3P, Benzamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]methyl]-4-chloro-N-methyl- 254741-13-4P, Benzamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]methyl]-2,3-difluoro-N-methyl- 254741-14-5P, Benzamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]methyl]-3,4-difluoro-N-methyl- 254741-15-6P, Benzamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]methyl]-3,5-difluoro-N-methyl- 254741-16-7P, Benzamide, 4-acetyl-N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]methyl]-N-methyl- 254741-17-8P, 2-Thiophenecarboxamide, N-[[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]methyl]-3-ethoxy-N-methyl- 254741-19-0P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-[(propylsulfonyl)amino]- 254741-20-3P, L-Valine, N-[[2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-N-(1-oxopentyl)-, methyl ester 254741-22-5P, L-Valine, N-[[2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-N-(1-oxopentyl)- 254741-24-7P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-2'-[(3,3-dimethyl-2-oxo-1-pyrrolidinyl)methyl]-4'-[(4-oxo-2-propyl-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]- 254741-26-9P, Butanamide, N-[[2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl]-4-[(2-ethyl-5,7-dimethyl-3H-imidazo[4,5-b]pyridin-3-yl)methyl][1,1'-biphenyl]-2-yl]methyl]-N,3,3-trimethyl- 254741-27-0P, Pentanamide, N-[(1S)-1-(aminocarbonyl)-2-methylpropyl]-N-[[2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]- 254741-28-1P, Pentanamide, N-[[2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-N-[(1S)-2-methyl-1-[(methylamino)carbonyl]propyl]- 254741-30-5P, Pentanamide, N-[(1S)-1-[(dimethylamino)carbonyl]-2-methylpropyl]-N-[[2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]- 254741-31-6P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-[[(2,2,2-trifluoroethyl)amino]methyl]- 254741-32-7P, [1,1'-Biphenyl]-2-carboxylic acid, 4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl]- 254741-33-8P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-(trifluoromethyl)- 254741-34-9P, [1,1'-Biphenyl]-2-carboxylic acid, 4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl]-, methyl ester 254741-35-0P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-(methoxymethyl)- 254741-36-1P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-fluoro- 254741-37-2P, [1,1'-Biphenyl]-2-sulfonamide, 2'-(cyanomethyl)-N-(4,5-dimethyl-3-isoxazolyl)-4'-[(2-ethyl-5,7-dimethyl-3H-imidazo[4,5-b]pyridin-3-yl)methyl]-

RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of N-isoxazolyl biphenylsulfonamides and related compds. as dual angiotensin II and endothelin receptor antagonists)

IT 254741-38-3P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-(cyanomethyl)-N-(4,5-dimethyl-3-isoxazolyl)- 254741-39-4P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-cyano-N-(4,5-dimethyl-3-isoxazolyl)- 254741-40-7P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-methyl- 254741-41-8P, [1,1'-Biphenyl]-2-sulfonamide, 2'-cyano-N-(4,5-dimethyl-3-isoxazolyl)-4'-[(2-ethyl-5,7-dimethyl-3H-imidazo[4,5-b]pyridin-3-yl)methyl]- 254741-42-9P, Pentanamide, N-[[2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl]-2-methyl[1,1'-biphenyl]-4-yl]methyl]-N-[(1S)-2-methyl-1-[(methylamino)carbonyl]propyl]- 254741-43-0P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-4'-[(2-ethyl-5,7-dimethyl-3H-imidazo[4,5-b]pyridin-3-yl)methyl]-2'-[[(2,2,2-trifluoroethyl)amino]methyl]- 254741-44-1P, Benzeneacetamide, N-[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]- 254741-45-2P, Butanamide, N-[4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-2-yl]-3,3-dimethyl- 254741-46-3P, [1,1'-Biphenyl]-2-sulfonamide, 2'-amino-4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)- 254741-48-5P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-nitro- 254741-50-9P, Pentanamide, 2-[[[2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl](1-oxopropyl)amino]-N,3-dimethyl-, (2S,3S)- 254741-52-1P, Cyclopropanecarboxamide, N-[[2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-N-[(1S,2S)-2-methyl-1-[(methylamino)carbonyl]butyl]- 254741-54-3P, Benzenepropanamide, N-[[2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-N-[(1S,2S)-2-methyl-1-[(methylamino)carbonyl]butyl]- 254741-56-5P, Pentanamide, 2-[[[2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl](3-methyl-1-oxobutyl)amino]-N,3-dimethyl-, (2S,3S)- 254741-58-7P, Hexanamide, N-[[2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-N-[(1S,2S)-2-methyl-1-[(methylamino)carbonyl]butyl]- 254741-60-1P, Pentanamide, 2-[[[2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl](1-oxobutyl)amino]-N,3-dimethyl-, (2S,3S)- 254741-62-3P, Pentanamide, 2-[[[2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl](1-oxopropyl)amino]-N,4-dimethyl-, (2S)- 254741-64-5P, Cyclopropanecarboxamide, N-[[2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-N-[(1S)-3-methyl-1-[(methylamino)carbonyl]butyl]- 254741-66-7P, Benzenepropanamide, N-[[2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-N-[(1S)-3-methyl-1-[(methylamino)carbonyl]butyl]- 254741-68-9P, Benzeneacetamide, N-[[2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-N-[(1S)-3-methyl-1-[(methylamino)carbonyl]butyl]- 254741-70-3P, Pentanamide, 2-[[[2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl](3-methyl-1-oxobutyl)amino]-N,4-dimethyl-, (2S)- 254741-72-5P, Hexanamide, N-[[2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-N-[(1S)-3-methyl-1-[(methylamino)carbonyl]butyl]- 254741-74-7P, Pentanamide, 2-[[[2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl](1-oxobutyl)amino]-N,4-dimethyl-, (2S)- 254741-76-9P, Butanamide, 2-[[[2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl](1-oxopropyl)amino]-N,3-dimethyl-, (2S)- 254741-78-1P, Cyclopropanecarboxamide,

N-[[2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-N-[(1S)-2-methyl-1-[(methylamino)carbonyl]propyl]- 254741-80-5P, Benzenepropanamide, N-[[2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-N-[(1S)-2-methyl-1-[(methylamino)carbonyl]propyl]- 254741-82-7P, Benzeneacetamide, N-[[2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-N-[(1S)-2-methyl-1-[(methylamino)carbonyl]propyl]- 254741-85-0P, Butanamide, N-[[2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-3-methyl-N-[(1S)-2-methyl-1-[(methylamino)carbonyl]propyl]- 254741-87-2P, Hexanamide, N-[[2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-N-[(1S)-2-methyl-1-[(methylamino)carbonyl]propyl]- 254741-89-4P, Butanamide, 2-[[[2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl](1-oxobutyl)amino]-N,3-dimethyl-, (2S)- 254741-91-8P, Pentanamide, N-[[2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-N-[(1S)-1-[(ethylamino)carbonyl]-2-methylpropyl]- 254741-93-0P, Pentanamide, N-[[2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-N-[(1S)-1-[(hexylamino)carbonyl]-2-methylpropyl]- 254741-95-2P, Pentanamide, N-[[2-cyano-2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-N-[(1S)-2-methyl-1-[(methylamino)carbonyl]propyl]- 254741-97-4P, Pentanamide, N-[[2-(cyanomethyl)-2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-N-[(1S)-2-methyl-1-[(methylamino)carbonyl]propyl]- 254741-99-6P, [1,1'-Biphenyl]-2-carboxamide, 4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl]- 254742-01-3P, [1,1'-Biphenyl]-2-carboxamide, 4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl]-N,N-dimethyl- 254742-03-5P, [1,1'-Biphenyl]-2-carboxamide, 4-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl]-N-methyl- 254742-05-7P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-2'-(methoxymethyl)-4'-[(5,6,7,8-tetrahydro-8-oxo-2-propyl-1(4H)-cycloheptimidazolyl)methyl]- 254742-06-8P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-4'-[[(3-methoxy-2,6-dimethyl-4-pyridinyl)oxy]methyl]-2'-methyl- 254742-07-9P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-2'-methyl-4'-[(5,6,7,8-tetrahydro-8-oxo-2-propyl-1(4H)-cycloheptimidazolyl)methyl]- 254742-08-0P, Butanamide, 2-[[[2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl]-2-(methoxymethyl)[1,1'-biphenyl]-4-yl]methyl](1-oxobutyl)amino]-N,3-dimethyl-, (2S)- 254742-09-1P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-2'-(hydroxymethyl)-4'-[(5,6,7,8-tetrahydro-8-oxo-2-propyl-1(4H)-cycloheptimidazolyl)methyl]- 254742-10-4P, [1,1'-Biphenyl]-2-sulfonamide, 2'-chloro-N-(4,5-dimethyl-3-isoxazolyl)-4'-[[(2-ethyl-5,6,7,8-tetrahydro-4-quinolinyl)oxy]methyl]- 254742-11-5P, Butanamide, 2-[[[2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl]-2-fluoro[1,1'-biphenyl]-4-yl]methyl](1-oxobutyl)amino]-N,3-dimethyl-, (2S)- 254742-12-6P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-(phenoxymethyl)- 254742-13-7P, Butanamide, 2-[[[2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl]-2-(1H-pyrazol-1-ylmethyl)[1,1'-biphenyl]-4-yl]methyl](1-oxobutyl)amino]-N,3-dimethyl-, (2S)- 254742-14-8P, Cyclopropanecarboxamide, N-[(1S)-1-[(dimethylamino)carbonyl]-2-methylpropyl]-N-[[2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]- 254742-15-9P, Butanamide, 2-[[[2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl](1-oxobutyl)amino]-N,N,3-trimethyl-, (2S)- 254742-16-0P, Cyclopropanecarboxamide, N-[(1S)-1-[(dimethylamino)carbonyl]-2-methylpropyl]-N-[[2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl]-2-(methoxymethyl)[1,1'-biphenyl]-4-yl]methyl]- 254742-17-1P, Butanamide, 2-[[[2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl]-2-(methoxymethyl)[1,1'-biphenyl]-4-yl]methyl](1-oxobutyl)amino]-N,N,3-trimethyl-, (2S) 254742-18-2P, Pentanamide, N-[[2-chloro-2'-[[(4,5-

dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-N-[(1S)-2-methyl-1-[(methylamino)carbonyl]propyl]- 254742-19-3P, Pentanamide, N-[[2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl]-2-(trifluoromethyl)[1,1'-biphenyl]-4-yl]methyl]-N-[(1S)-2-methyl-1-[(methylamino)carbonyl]propyl]- 254742-20-6P, Cyclobutanecarboxamide, N-[[2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-N-[(1S)-2-methyl-1-[(methylamino)carbonyl]propyl]- 254742-21-7P, 1H-Imidazole-5-carboxylic acid, 1-[[2-chloro-2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-4-ethyl-2-propyl- 254742-22-8P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-[(methylsulfonyl)amino]- 254742-23-9P, Pentanamide, N-[[2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-N-[(1S)-2-methyl-1-[(4-methyl-1-piperazinyl)carbonyl]propyl]- 254742-24-0P, Pentanamide, N-[[2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-N-[(1S)-2-methyl-1-(1-piperidinylcarbonyl)propyl]- 254742-25-1P, Pentanamide, N-[(1S)-1-[[(3,3-dimethylbutyl)amino]carbonyl]-2-methylpropyl]-N-[[2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]- 254742-28-4P, Pentanamide, N-[[2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-N-[(1S)-1-[[[(4-fluorophenyl)methyl]amino]carbonyl]-2-methylpropyl]- 254742-29-5P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-[(1-methylethoxy)methyl]- 254742-31-9P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-(propoxymethyl)- 254742-33-1P, 1H-Imidazole-5-carboxamide, 4-chloro-1-[[2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-2-propyl- 254742-35-3P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-2'-fluoro-4'-[(5,6,7,8-tetrahydro-8-oxo-2-propyl-1(4H)-cycloheptimidazolyl)methyl]- 254742-36-4P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-[(2-oxo-1(2H)-pyridinyl)methyl]- 254742-37-5P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-(1H-pyrazol-1-ylmethyl)- 254742-38-6P, 1H-Imidazole-5-carboxamide, 2-butyl-4-chloro-1-[[2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]- 254742-39-7P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-4'-[[(2-methyl-4-quinolinyl)oxy]methyl]- 254742-41-1P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-4'-[[(2-ethyl-4-quinolinyl)oxy]methyl]- 254742-43-3P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-4'-[[(2-ethyl-5,6,7,8-tetrahydro-4-quinolinyl)oxy]methyl]- 254742-45-5P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-4'-[[(2-propyl-4-quinolinyl)oxy]methyl]- 254742-46-6P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(6,7-dihydro-2,4-dimethyl-7-oxopyrido[2,3-d]pyrimidin-8(5H)-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)- 254742-47-7P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-2'-[(3,3-dimethyl-2-oxo-1-pyrrolidinyl)methyl]-4'-[[(2-ethyl-4-quinolinyl)oxy]methyl]- 254742-49-9P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-2'-[(3,3-dimethyl-2-oxo-1-pyrrolidinyl)methyl]-4'-[[(2-ethyl-5,6,7,8-tetrahydro-4-quinolinyl)oxy]methyl]- 254742-51-3P, 1H-Benzimidazole-7-carboxamide, 1-[[2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-2-ethyl-N-methyl- 254742-53-5P, 1H-Benzimidazole-7-carboxylic acid, 1-[[2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-2-ethyl-, phenylmethyl ester 254742-54-6P, 1H-Benzimidazole-7-carboxylic acid, 1-[[2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-2-ethyl-, 2-phenylethyl ester 254742-56-8P, 1H-Benzimidazole-7-carboxylic acid, 1-[[2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-2-ethyl-, 2-(2-oxo-1-pyrrolidinyl)ethyl ester 254742-58-0P,

1H-Benzimidazole-7-carboxylic acid, 1-[[2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-2-ethyl-, 3-(2-oxo-1-pyrrolidinyl)propyl ester 254742-60-4P, [1,1'-Biphenyl]-2-sulfonamide, 2'-cyano-N-(4,5-dimethyl-3-isoxazolyl)-4'-[[(2-ethyl-4-quinolinyl)oxy]methyl]- 254742-62-6P, [1,1'-Biphenyl]-2-sulfonamide, 2'-(cyanomethyl)-N-(4,5-dimethyl-3-isoxazolyl)-4'-[(5,6,7,8-tetrahydro-8-oxo-2-propyl-1(4H)-cycloheptimidazolyl)methyl]- 254742-64-8P, 1H-Imidazole-5-carboxamide, 1-[[2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-4-ethyl-N-methyl-2-propyl- 254742-65-9P, 1H-Imidazole-5-carboxamide, 1-[[2-chloro-2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-4-ethyl-2-propyl- 254742-66-0P, 1H-Imidazole-5-carboxamide, 1-[[2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-4-ethyl-2-propyl- 254742-67-1P, 1H-Benzimidazole-7-carboxamide, 1-[[2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-2-ethoxy-N-methyl- 254742-68-2P, 1H-Benzimidazole-7-carboxamide, 1-[[2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-2-ethoxy-N,N-dimethyl- 254742-69-3P, 3-Pyridinecarboxylic acid, 2-[[[2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]propylamino]- 254742-70-6P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(3,5-dibutyl-1H-1,2,4-triazol-1-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)- 254742-71-7P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-4'-[(5,6,7,8-tetrahydro-8-oxo-2-propyl-1(4H)-cycloheptimidazolyl)methyl]- 254742-72-8P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2,7-diethyl-5H-pyrazolo[1,5-b][1,2,4]triazol-5-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)- 254742-73-9P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[[2-butyl-6-[[[methyl(1-methylethyl)amino]carbonyl]amino]-4-oxo-3(4H)-quinazolinyl]methyl]-N-(4,5-dimethyl-3-isoxazolyl)- 254742-75-1P, 3-Pyridinecarboxamide, 2-[[[2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]propylamino]-N-methyl- 254742-76-2P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-4'-[[(3-methoxy-2,6-dimethyl-4-pyridinyl)oxy]methyl]- 254742-77-3P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-2'-[(3,3-dimethyl-2-oxo-1-pyrrolidinyl)methyl]-4'-[[(3-methoxy-2,6-dimethyl-4-pyridinyl)oxy]methyl]- 254742-78-4P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-2'-[(3,3-dimethyl-2-oxo-1-pyrrolidinyl)methyl]-4'-[(5,6,7,8-tetrahydro-8-oxo-2-propyl-1(4H)-cycloheptimidazolyl)methyl]- 254742-79-5P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-4'-[[(3-methoxy-2,6-dimethyl-4-pyridinyl)oxy]methyl]-2'-(methoxymethyl)- 254742-80-8P, 1H-Imidazole-5-carboxamide, 1-[[2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-2-ethyl-4-methyl- 254742-81-9P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-3(4H)-quinazolinyl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)- 254742-82-0P, Pentanamide, N-[[2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl]-2-[(3,3-dimethyl-2-oxo-1-pyrrolidinyl)methyl][1,1'-biphenyl]-4-yl]methyl]-N-[(1S)-2-methyl-1-[(methylamino)carbonyl]propyl]- 254742-83-1P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-[(4,4-dimethyl-2-oxo-1-pyrrolidinyl)methyl]- 254742-84-2P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(3,5-dibutyl-1H-1,2,4-triazol-1-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-[(3,3-dimethyl-2-oxo-1-pyrrolidinyl)methyl]- 254742-85-3P, Acetamide, N-[2-[[[2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl]-4-[(2-ethyl-5,7-dimethyl-3H-imidazo[4,5-b]pyridin-3-yl)methyl][1,1'-biphenyl]-2-yl]methyl]methylamino]ethyl]- 254742-86-4P, [1,1'-Biphenyl]-2-acetic acid, 2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl]-4-[(2-ethyl-5,7-dimethyl-3H-imidazo[4,5-b]pyridin-3-yl)methyl]-, ethyl ester 254742-87-5P, Pentanamide, N-[[2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-N-[(1S)-2-methyl-1-[(propylamino)carbonyl]propyl]- 254742-88-6P, Pentanamide, N-[[2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-N-[(1S)-2-methyl-1-[[[(tetrahydro-2-furanyl)methyl]amino]carbonyl]propyl]- 254742-89-7P

, [1,1'-Biphenyl]-2-sulfonamide, 2'-chloro-N-(4,5-dimethyl-3-isoxazolyl)-4'-[[(2-ethyl-4-quinolinyl)oxy]methyl]- 254742-91-1P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-4'-[[(2-ethyl-4-quinolinyl)oxy]methyl]-2'-(trifluoromethyl)- 254742-92-2P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-chloro-N-(4,5-dimethyl-3-isoxazolyl)- 254742-93-3P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-[(2-methylpropoxy)methyl]- 254742-94-4P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-[(ethylsulfonyl)amino]- 254742-95-5P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-[(2,2,2-trifluoroethoxy)methyl]- 254742-96-6P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-[(2-fluoroethoxy)methyl]- 254742-97-7P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-2'-(ethoxymethyl)-4'-[[(3-methoxy-2,6-dimethyl-4-pyridinyl)oxy]methyl]- 254742-98-8P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-2'-(ethoxymethyl)-4'-[(5,6,7,8-tetrahydro-8-oxo-2-propyl-1(4H)-cycloheptimidazolyl)methyl]- 254742-99-9P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-(3,3,3-trifluoropropyl)- 254743-00-5P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-(3-fluoropropyl)- 254743-01-6P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-(1,1-difluoroethyl)-N-(4,5-dimethyl-3-isoxazolyl)- 254743-03-8P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-(2,2,2-trifluoroethyl)- 254743-05-0P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-(2-methylpropoxy)- 254743-06-1P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-(2-methoxyethoxy)- 254743-08-3P, [1,1'-Biphenyl]-2-sulfonamide, 2'-butyl-4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)- 254743-10-7P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-[(methoxymethylamino)methyl]- 254743-12-9P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[(2,2-difluoroethoxy)methyl]-N-(4,5-dimethyl-3-isoxazolyl)- 254743-15-2P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-(2-fluoroethyl)- 254743-16-3P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-(2-hydroxyethyl)- 254743-17-4P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-(3-methylbutyl)- 254743-18-5P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-(2-methylpropyl)- 254743-19-6P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[[2-(3,3-difluorobutyl)-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl]methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-(ethoxymethyl)- 254743-20-9P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-4'-[[(3-methoxy-2,6-dimethyl-4-pyridinyl)oxy]methyl]-2'-(3,3,3-trifluoropropyl)- 254743-22-1P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-[(1,1-dimethylethoxy)methyl]-N-(4,5-dimethyl-3-isoxazolyl)- 254743-24-3P, 1H-Imidazole-5-carboxamide, 1-[[2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl]-2-(methoxymethyl)[1,1'-biphenyl]-4-yl]methyl]-4-ethyl-2-propyl- 254743-25-4P, 1H-Imidazole-5-carboxamide, 1-[[2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl]-2-(methoxymethyl)[1,1'-biphenyl]-4-yl]methyl]-4-ethyl-N-methyl-2-propyl- 254743-26-5P, 1H-Imidazole-5-carboxamide,

1-[[2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl]-2-methyl[1,1'-biphenyl]-4-yl]methyl]-4-ethyl-2-propyl- 254743-27-6P, 1H-Imidazole-5-carboxamide, 1-[[2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl]-2-methyl[1,1'-biphenyl]-4-yl]methyl]-4-ethyl-N-methyl-2-propyl- 254743-28-7P 254743-29-8P 254743-30-1P 254743-31-2P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-ethyl- 254743-32-3P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-(2,2-dimethylpropyl)- 254743-33-4P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-(2-ethoxyethyl)- 254743-34-5P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-2'-ethyl-4'-[[(3-methoxy-2,6-dimethyl-4-pyridinyl)oxy]methyl]- 254743-35-6P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-2'-(2,2-dimethylpropyl)-4'-[[(3-methoxy-2,6-dimethyl-4-pyridinyl)oxy]methyl]- 254743-36-7P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-2'-(2-ethoxyethyl)-4'-[[(3-methoxy-2,6-dimethyl-4-pyridinyl)oxy]methyl]- 254743-37-8P, [1,1'-Biphenyl]-2-sulfonamide, 2'-[(1,1-dimethylethoxy)methyl]-N-(3,4-dimethyl-5-isoxazolyl)-4'-[[(3-methoxy-2,6-dimethyl-4-pyridinyl)oxy]methyl]- 254743-38-9P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-2'-ethyl-4'-[[(3-methoxy-2,6-dimethyl-4-pyridinyl)oxy]methyl]- 254743-39-0P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-2'-(2,2-dimethylpropyl)-4'-[[(3-methoxy-2,6-dimethyl-4-pyridinyl)oxy]methyl]- 254743-40-3P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-2'-(2-ethoxyethyl)-4'-[[(3-methoxy-2,6-dimethyl-4-pyridinyl)oxy]methyl]- 254743-41-4P, [1,1'-Biphenyl]-2-sulfonamide, 2'-[(1,1-dimethylethoxy)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-4'-[[(3-methoxy-2,6-dimethyl-4-pyridinyl)oxy]methyl]- 254743-42-5P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-2'-ethyl-4'-[(5,6,7,8-tetrahydro-8-oxo-2-propyl-1(4H)-cycloheptimidazolyl)methyl]- 254743-43-6P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-2'-(2,2-dimethylpropyl)-4'-[(5,6,7,8-tetrahydro-8-oxo-2-propyl-1(4H)-cycloheptimidazolyl)methyl]- 254743-44-7P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-2'-(2-ethoxyethyl)-4'-[(5,6,7,8-tetrahydro-8-oxo-2-propyl-1(4H)-cycloheptimidazolyl)methyl]- 254743-45-8P, [1,1'-Biphenyl]-2-sulfonamide, 2'-[(1,1-dimethylethoxy)methyl]-N-(3,4-dimethyl-5-isoxazolyl)-4'-[(5,6,7,8-tetrahydro-8-oxo-2-propyl-1(4H)-cycloheptimidazolyl)methyl]- 254743-46-9P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-2'-ethyl-4'-[(5,6,7,8-tetrahydro-8-oxo-2-propyl-1(4H)-cycloheptimidazolyl)methyl]- 254743-47-0P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-2'-(2,2-dimethylpropyl)-4'-[(5,6,7,8-tetrahydro-8-oxo-2-propyl-1(4H)-cycloheptimidazolyl)methyl]- 254743-48-1P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-2'-(2-ethoxyethyl)-4'-[(5,6,7,8-tetrahydro-8-oxo-2-propyl-1(4H)-cycloheptimidazolyl)methyl]- 254743-49-2P, [1,1'-Biphenyl]-2-sulfonamide, 2'-[(1,1-dimethylethoxy)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-4'-[(5,6,7,8-tetrahydro-8-oxo-2-propyl-1(4H)-cycloheptimidazolyl)methyl]- 254743-50-5P 254743-51-6P 254743-53-8P 254743-56-1P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-2'-(1-hydroxyethyl)-4'-[[(3-methoxy-2,6-dimethyl-4-pyridinyl)oxy]methyl]- 254743-57-2P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-2'-(1-hydroxy-1-methylethyl)-4'-[[(3-methoxy-2,6-dimethyl-4-pyridinyl)oxy]methyl]- 254743-58-3P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-4'-[[(3-methoxy-2,6-dimethyl-4-pyridinyl)oxy]methyl]-2'-(tetrahydro-2-furanyl)- 254743-59-4P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-2'-(1-hydroxyethyl)-4'-[(5,6,7,8-tetrahydro-8-oxo-2-propyl-1(4H)-cycloheptimidazolyl)methyl]- 254743-61-8P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-2'-(1-hydroxy-1-methylethyl)-4'-[(5,6,7,8-tetrahydro-8-oxo-2-propyl-1(4H)-cycloheptimidazolyl)methyl]-

254743-62-9P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-2'-(tetrahydro-2-furanyl)-4'-[(5,6,7,8-tetrahydro-8-oxo-2-propyl-1(4H)-cycloheptimidazolyl)methyl]- 254743-63-0P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-(1-hydroxyethyl)- 254743-64-1P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-(1-hydroxy-1-methylethyl)- 254743-65-2P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-(tetrahydro-2-furanyl)- 254743-66-3P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-2'-(1-hydroxyethyl)-4'-[[(3-methoxy-2,6-dimethyl-4-pyridinyl)oxy]methyl]- 254743-67-4P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-2'-(1-hydroxy-1-methylethyl)-4'-[[(3-methoxy-2,6-dimethyl-4-pyridinyl)oxy]methyl]- 254743-68-5P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-4'-[[(3-methoxy-2,6-dimethyl-4-pyridinyl)oxy]methyl]-2'-(tetrahydro-2-furanyl)- 254743-69-6P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-2'-(1-hydroxyethyl)-4'-[(5,6,7,8-tetrahydro-8-oxo-2-propyl-1(4H)-cycloheptimidazolyl)methyl]- 254743-70-9P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-2'-(1-hydroxy-1-methylethyl)-4'-[(5,6,7,8-tetrahydro-8-oxo-2-propyl-1(4H)-cycloheptimidazolyl)methyl]- 254743-71-0P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-2'-(tetrahydro-2-furanyl)-4'-[(5,6,7,8-tetrahydro-8-oxo-2-propyl-1(4H)-cycloheptimidazolyl)methyl]- 254743-72-1P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-4'-[(5,6,7,8-tetrahydro-8-oxo-2-propyl-1(4H)-cycloheptimidazolyl)methyl]-2'-(3,3,3-trifluoropropyl)- 254743-73-2P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-4'-[(5,6,7,8-tetrahydro-8-oxo-2-propyl-1(4H)-cycloheptimidazolyl)methyl]-2'-(3,3,3-trifluoropropyl)- 254743-74-3P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-4'-[[(3-methoxy-2,6-dimethyl-4-pyridinyl)oxy]methyl]-2'-propyl- 254743-75-4P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-4'-[[(3-methoxy-2,6-dimethyl-4-pyridinyl)oxy]methyl]-2'-propyl- 254743-76-5P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-2'-propyl-4'-[(5,6,7,8-tetrahydro-8-oxo-2-propyl-1(4H)-cycloheptimidazolyl)methyl]- 254743-77-6P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-2'-propyl-4'-[(5,6,7,8-tetrahydro-8-oxo-2-propyl-1(4H)-cycloheptimidazolyl)methyl]- 254743-78-7P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-2'-[(2-fluoroethoxy)methyl]-4'-[[(3-methoxy-2,6-dimethyl-4-pyridinyl)oxy]methyl]-
RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of N-isoxazolyl biphenylsulfonamides and related compds. as dual angiotensin II and endothelin receptor antagonists)

IT 254743-79-8P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-2'-[(2-fluoroethoxy)methyl]-4'-[[(3-methoxy-2,6-dimethyl-4-pyridinyl)oxy]methyl]- 254743-80-1P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-2'-[(2-fluoroethoxy)methyl]-4'-[(5,6,7,8-tetrahydro-8-oxo-2-propyl-1(4H)-cycloheptimidazolyl)methyl]- 254743-81-2P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-2'-[(2-fluoroethoxy)methyl]-4'-[(5,6,7,8-tetrahydro-8-oxo-2-propyl-1(4H)-cycloheptimidazolyl)methyl]- 254743-82-3P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[[2-(2,2-difluorobutyl)-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl]methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-propyl- 254743-83-4P 254743-84-5P 254743-85-6P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-2'-(ethoxymethyl)-4'-[[4-oxo-2-(4,4,4-trifluorobutyl)-1,3-diazaspiro[4.4]non-1-en-3-yl]methyl]- 254743-86-7P 254743-87-8P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-4'-[[4-oxo-2-(4,4,4-trifluorobutyl)-1,3-diazaspiro[4.4]non-1-en-3-yl]methyl]-2'-propyl- 254743-88-9P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-2'-(ethoxymethyl)-4'-[[4-oxo-2-(3,3,3-trifluoropropyl)-1,3-diazaspiro[4.4]non-1-en-3-yl]methyl]- 254743-89-0P

254743-90-3P 254743-91-4P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-4'-[[4-oxo-2-(3,3,3-trifluoropropyl)-1,3-diazaspiro[4.4]non-1-en-3-yl]methyl]-2'-propyl- 254743-92-5P, [1,1'-Biphenyl]-2-sulfonamide, 2'-(1,1-difluoropropyl)-N-(3,4-dimethyl-5-isoxazolyl)-4'-[[(3-methoxy-2,6-dimethyl-4-pyridinyl)oxy]methyl]- 254743-93-6P, [1,1'-Biphenyl]-2-sulfonamide, 2'-(1,1-difluoropropyl)-N-(4,5-dimethyl-3-isoxazolyl)-4'-[[(3-methoxy-2,6-dimethyl-4-pyridinyl)oxy]methyl]- 254743-94-7P, [1,1'-Biphenyl]-2-sulfonamide, 2'-(1,1-difluoropropyl)-N-(4,5-dimethyl-3-isoxazolyl)-4'-[(5,6,7,8-tetrahydro-8-oxo-2-propyl-1(4H)-cycloheptimidazolyl)methyl]- 254743-95-8P, [1,1'-Biphenyl]-2-sulfonamide, 2'-(1,1-difluoropropyl)-N-(3,4-dimethyl-5-isoxazolyl)-4'-[(5,6,7,8-tetrahydro-8-oxo-2-propyl-1(4H)-cycloheptimidazolyl)methyl]- 254743-96-9P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-(1,1,3,3,3-pentafluoropropyl)- 254743-97-0P 254743-98-1P, 1H-Imidazole-5-carboxamide, 1-[[2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl]-2-ethyl[1,1'-biphenyl]-4-yl]methyl]-4-ethyl-N-methyl-2-propyl- 254743-99-2P, 1H-Imidazole-5-carboxamide, 1-[[2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl]-2-propyl[1,1'-biphenyl]-4-yl]methyl]-4-ethyl-N-methyl-2-propyl- 254744-00-8P, 1H-Imidazole-5-carboxamide, 1-[[2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl]-2-[(2-fluoroethoxy)methyl][1,1'-biphenyl]-4-yl]methyl]-4-ethyl-N-methyl-2-propyl- 254744-01-9P, 1H-Imidazole-5-carboxamide, 1-[[2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl]-2-(ethoxymethyl)[1,1'-biphenyl]-4-yl]methyl]-4-ethyl-N-methyl-2-propyl- 254744-02-0P, 1H-Imidazole-5-carboxamide, 1-[[2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl]-2-ethyl[1,1'-biphenyl]-4-yl]methyl]-4-ethyl-2-propyl- 254744-03-1P, 1H-Imidazole-5-carboxamide, 1-[[2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl]-2-propyl[1,1'-biphenyl]-4-yl]methyl]-4-ethyl-2-propyl- 254744-04-2P, 1H-Imidazole-5-carboxamide, 1-[[2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl]-2-[(2-fluoroethoxy)methyl][1,1'-biphenyl]-4-yl]methyl]-4-ethyl-2-propyl- 254744-05-3P, 1H-Imidazole-5-carboxamide, 1-[[2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl]-2-(ethoxymethyl)[1,1'-biphenyl]-4-yl]methyl]-4-ethyl-2-propyl- 254744-06-4P, 1H-Imidazole-5-carboxamide, 1-[[2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl]-2-ethyl[1,1'-biphenyl]-4-yl]methyl]-4-ethyl-N-methyl-2-propyl- 254744-07-5P, 1H-Imidazole-5-carboxamide, 1-[[2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl]-2-propyl[1,1'-biphenyl]-4-yl]methyl]-4-ethyl-N-methyl-2-propyl- 254744-08-6P, 1H-Imidazole-5-carboxamide, 1-[[2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl]-2-[(2-fluoroethoxy)methyl][1,1'-biphenyl]-4-yl]methyl]-4-ethyl-N-methyl-2-propyl- 254744-09-7P, 1H-Imidazole-5-carboxamide, 1-[[2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl]-2-(ethoxymethyl)[1,1'-biphenyl]-4-yl]methyl]-4-ethyl-N-methyl-2-propyl- 254744-10-0P, 1H-Imidazole-5-carboxamide, 1-[[2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl]-2-ethyl[1,1'-biphenyl]-4-yl]methyl]-4-ethyl-2-propyl- 254744-11-1P, 1H-Imidazole-5-carboxamide, 1-[[2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl]-2-propyl[1,1'-biphenyl]-4-yl]methyl]-4-ethyl-2-propyl- 254744-12-2P, 1H-Imidazole-5-carboxamide, 1-[[2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl]-2-[(2-fluoroethoxy)methyl][1,1'-biphenyl]-4-yl]methyl]-4-ethyl-2-propyl- 254744-13-3P, 1H-Imidazole-5-carboxamide, 1-[[2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulfonyl]-2-(ethoxymethyl)[1,1'-biphenyl]-4-yl]methyl]-4-ethyl-2-propyl-
RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of N-isoxazolyl biphenylsulfonamides and related compds. as dual angiotensin II and endothelin receptor antagonists)

IT 56-12-2, 4-Aminobutyric acid, reactions 75-03-6, Iodoethane 78-09-1, Tetraethyl orthocarbonate 79-03-8, Propionyl chloride 79-44-7, Dimethylcarbamyl chloride 95-89-6, 2-Chloro-3,6-dimethylpyrazine

109-81-9, N-Methylethylenediamine 124-40-3, Dimethylamine, reactions 127-08-2, Potassium acetate 541-41-3, Ethyl chloroformate 543-27-1, Isobutyl chloroformate 589-15-1, 4-Bromobenzyl bromide 627-03-2, Ethoxyacetic acid 638-29-9, Valeryl chloride 676-58-4, Methylmagnesium chloride 680-15-9, Acetic acid, difluoro(fluorosulfonyl)-, methyl ester 767-00-0, 4-Cyanophenol 865-33-8, Potassium methoxide 873-75-6, 4-Bromobenzyl alcohol 1117-97-1, N-Methoxy-N-methylamine 1122-91-4, 4-Bromobenzaldehyde 1450-75-5, Ethanone, 1-(5-bromo-2-hydroxyphenyl)- 1530-32-1, Ethyltriphenylphosphonium bromide 1609-86-5, tert-Butyl isocyanate 2835-98-5, Phenol, 2-amino-5-methyl- 2905-25-1, 2-Bromobenzenesulfonyl chloride 3959-07-7, 4-Bromobenzylamine 4858-85-9, 2,3-Dichloropyrazine 5326-34-1, 4-Bromo-3-nitrotoluene 6228-47-3, Propyltriphenylphosphonium bromide 6482-24-2, 1-Bromo-2-methoxyethane 13734-41-3, L-Valine, N-[(1,1-dimethylethoxy)carbonyl]- 14508-49-7, 2-Chloropyrazine 14678-02-5, 5-Amino-3-methylisoxazole 22059-22-9, Acetamide oxime 22884-29-3, Isobutyltriphenylphosphonium bromide 28466-21-9, 4-Amino-1,3,5-trimethylpyrazole 29006-02-8, Butanoic acid, 4-methoxy- 33670-32-5, Methoxymethyltriphenylphosphonium bromide 34328-47-7, Benzaldehyde, 4-bromo-3-(trifluoromethyl)- 34841-06-0, 3-Bromo-4-methoxybenzaldehyde 40155-28-0, 2-Chloro-3-methoxypyrazine 41963-20-6, 4-Bromo-3-methylbenzonitrile 53553-14-3, Methyl 2-chloro-3-nitrobenzoate 53596-60-4, Benzoic acid, 4-hydroxy-3-(2-propenyl)-, methyl ester 60421-23-0, Cyclopentanecarboxylic acid, 1-amino-, methyl ester, hydrochloride 74410-26-7, Butanamide, 2-amino-N,3-dimethyl-, monohydrochloride, (2S)- 76513-69-4, 2-(Trimethylsilyl)ethoxymethyl chloride 78775-11-8, Benzaldehyde, 4-bromo-3-methyl- 87199-17-5, 4-Formylphenylboronic acid 89464-87-9, 2-Amino-3-methoxy-5-methylpyrazine 98946-18-0, tert-Butyl 2,2,2-trichloroacetimidate 109072-25-5, 4(1H)-Quinolinone, 2-ethyl- 120077-69-2, Benzaldehyde, 4-bromo-3-chloro- 124750-49-8, 1H-Imidazole-4-carboxaldehyde, 5-chloro-2-propyl- 125110-82-9, 4,4-Difluoropentanoic acid 133059-43-5, Benzaldehyde, 4-bromo-3-fluoro- 133240-06-9, 1H-Imidazo[4,5-b]pyridine, 2-ethyl-5,7-dimethyl- 138402-05-8, 1,3-Diazaspiro[4.4]non-1-en-4-one, 2-butyl- 148547-19-7, Methyl 4-bromo-3-methylbenzoate 150691-04-6, Boronic acid, [2-[[(1,1-dimethylethyl)amino]sulfonyl]phenyl]- 151257-01-1, 1,3-Diazaspiro[4.4]non-1-en-4-one, 2-butyl-, monohydrochloride 153039-15-7, Butanoic acid, 4-amino-2,2-dimethyl-, hydrochloride 160313-50-8, Benzonitrile, 4-bromo-3-(1,3-dioxolan-2-yl)- 162647-41-8, 4-Pyridinol, 3-methoxy-2,6-dimethyl- 167985-34-4, 1H-Imidazole-4-carboxylic acid, 5-ethyl-2-propyl-, ethyl ester 176961-13-0, Boronic acid, [2-[[(3,4-dimethyl-5-isoxazolyl)[(2-methoxyethoxy)methyl]amino]sulfonyl]phenyl]- 195436-86-3, Benzenesulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-N-[(2-methoxyethoxy)methyl]-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)- 254746-77-5, Boronic acid, [2-[[(4,5-dimethyl-3-isoxazolyl)[(2-methoxyethoxy)methyl]amino]sulfonyl]phenyl]- 254746-78-6, Butanoic acid, 4-amino-2,2-dimethyl-, ethyl ester, hydrochloride 254746-79-7, Boronic acid, [2-[[(3,4-dimethyl-5-isoxazolyl)[[2-[(trimethylsilyl)oxy]ethoxy]methyl]amino]sulfonyl]phenyl]- 254746-80-0, [1,1'-Biphenyl]-2-sulfonamide, 4'-(bromomethyl)-N-(3,4-dimethyl-5-isoxazolyl)-2'-(ethoxymethyl)-N-[(2-methoxyethoxy)methyl]- 254746-81-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of N-isoxazolyl biphenylsulfonamides and related compds. as dual angiotensin II and endothelin receptor antagonists)

IT 14847-51-9P, Phenol, 2-bromo-5-methyl- 79047-47-5P, 1H-Imidazole-4-methanol, 5-chloro-2-propyl- 89003-95-2P, Benzonitrile, 4-bromo-3-formyl- 123652-98-2P, Benzene, 2-bromo-4-(dimethoxymethyl)-1-methoxy- 142031-67-2P, Benzoic acid, 4-bromo-3-(bromomethyl)-, methyl ester 160313-48-4P, Benzenemethanol, 4-bromo-3-(1,3-dioxolan-2-yl)- 176961-30-1P, [1,1'-Biphenyl]-2-sulfonamide, 4'-(bromomethyl)-N-(3,4-dimethyl-5-isoxazolyl)-N-[(2-methoxyethoxy)methyl]- 189762-06-9P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-4'-formyl-N-

[(2-methoxyethoxy)methyl]- 189762-08-1P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-4'-formyl- 190197-86-5P, Benzonitrile, 4-bromo-3-(bromomethyl)- 254744-14-4P, Benzonitrile, 3-[(acetyloxy)methyl]-4-bromo- 254744-15-5P, Benzaldehyde, 4-bromo-3-(hydroxymethyl)- 254744-16-6P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-4'-formyl-2'-(hydroxymethyl)-N-[[2-[(trimethylsilyl)oxy]ethoxy]methyl]- 254744-17-7P, Benzonitrile, 4-bromo-3-(methoxymethyl)- 254744-18-8P, Benzaldehyde, 4-bromo-3-(methoxymethyl)- 254744-19-9P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-4'-formyl-N-[(2-methoxyethoxy)methyl]-2'-(methoxymethyl)- 254744-20-2P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-4'-(hydroxymethyl)-N-[(2-methoxyethoxy)methyl]-2'-(methoxymethyl)- 254744-21-3P, [1,1'-Biphenyl]-2-sulfonamide, 4'-(bromomethyl)-N-(3,4-dimethyl-5-isoxazolyl)-N-[(2-methoxyethoxy)methyl]-2'-(methoxymethyl)- 254744-22-4P, [1,1'-Biphenyl]-2-sulfonamide, 2'-cyano-N-(3,4-dimethyl-5-isoxazolyl)-4'-(hydroxymethyl)-N-[[2-[(trimethylsilyl)oxy]ethoxy]methyl]- 254744-23-5P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-2'-formyl-4'-(hydroxymethyl)-N-[[2-[(trimethylsilyl)oxy]ethoxy]methyl]- 254744-24-6P, [1,1'-Biphenyl]-2-sulfonamide, 2'-chloro-N-(3,4-dimethyl-5-isoxazolyl)-4'-formyl-N-[[2-[(trimethylsilyl)oxy]ethoxy]methyl]- 254744-25-7P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-4'-formyl-2'-(trifluoromethyl)-N-[[2-[(trimethylsilyl)oxy]ethoxy]methyl]- 254744-26-8P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-4'-formyl-N-[(2-methoxyethoxy)methyl]-2'-methyl- 254744-27-9P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-2'-fluoro-4'-formyl-N-[(2-methoxyethoxy)methyl]- 254744-28-0P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-4'-[[(methylsulfonyl)oxy]methyl]-2'-(trifluoromethyl)-N-[[2-[(trimethylsilyl)oxy]ethoxy]methyl]- 254744-29-1P, [1,1'-Biphenyl]-2-sulfonamide, 2'-chloro-N-(3,4-dimethyl-5-isoxazolyl)-4'-[[(methylsulfonyl)oxy]methyl]-N-[[2-[(trimethylsilyl)oxy]ethoxy]methyl]- 254744-30-4P, [1,1'-Biphenyl]-2-sulfonamide, 4'-(bromomethyl)-N-(3,4-dimethyl-5-isoxazolyl)-2'-fluoro-N-[(2-methoxyethoxy)methyl]- 254744-31-5P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-4'-(hydroxymethyl)-2'-[[(methylsulfonyl)oxy]methyl]-N-[[2-[(trimethylsilyl)oxy]ethoxy]methyl]- 254744-32-6P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-N-[(2-methoxyethoxy)methyl]-2'-methyl-4'-[[(methylsulfonyl)oxy]methyl]- 254744-33-7P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-2'-(hydroxymethyl)-4'-[[(methylsulfonyl)oxy]methyl]-N-[[2-[(trimethylsilyl)oxy]ethoxy]methyl]- 254744-34-8P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-4'-formyl-2'-methyl-N-[[2-[(trimethylsilyl)oxy]ethoxy]methyl]- 254744-35-9P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-4'-formyl-N-[[2-[(trimethylsilyl)oxy]ethoxy]methyl]- 254744-36-0P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-4'-[[(methylsulfonyl)oxy]methyl]-N-[[2-[(trimethylsilyl)oxy]ethoxy]methyl]- 254744-37-1P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-4'-formyl-2'-(methoxymethyl)-N-[[2-[(trimethylsilyl)oxy]ethoxy]methyl]- 254744-38-2P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-2'-formyl-4'-(hydroxymethyl)-N-[(2-methoxyethoxy)methyl]- 254744-39-3P 254744-40-6P, [1,1'-Biphenyl]-2-sulfonamide, N-(4,5-dimethyl-3-isoxazolyl)-4'-(hydroxymethyl)-N-[(2-methoxyethoxy)methyl]- 254744-41-7P, [1,1'-Biphenyl]-2-sulfonamide, 4'-(bromomethyl)-N-(4,5-dimethyl-3-isoxazolyl)-N-[(2-methoxyethoxy)methyl]- 254744-42-8P 254744-43-9P, [1,1'-Biphenyl]-2-sulfonamide, 4'-cyano-N-(3,4-dimethyl-5-isoxazolyl)-2'-formyl-N-[(2-methoxyethoxy)methyl]- 254744-44-0P, [1,1'-Biphenyl]-2-sulfonamide, 4'-cyano-N-(3,4-dimethyl-5-isoxazolyl)-N-[(2-methoxyethoxy)methyl]-2'-[(methylamino)methyl]- 254744-45-1P, Carbamic acid, [[4-cyano-2'-[[(3,4-dimethyl-5-isoxazolyl)[(2-methoxyethoxy)methyl]amino]sulfonyl][1,1'-biphenyl]-2-yl]methyl]methyl-, 1,1-dimethylethyl ester 254744-46-2P, Carbamic acid,

[[2'-[[(3,4-dimethyl-5-isoxazolyl)[(2-methoxyethoxy)methyl]amino]sulfonyl]-4-formyl[1,1'-biphenyl]-2-yl]methyl]methyl-, 1,1-dimethylethyl ester 254744-47-3P, Carbamic acid, [[4-(bromomethyl)-2'-[[(3,4-dimethyl-5-isoxazolyl)[(2-methoxyethoxy)methyl]amino]sulfonyl][1,1'-biphenyl]-2-yl]methyl]methyl-, 1,1-dimethylethyl ester 254744-48-4P 254744-49-5P, [1,1'-Biphenyl]-2-sulfonamide, 4'-cyano-N-(3,4-dimethyl-5-isoxazolyl)-2'-(1,3-dioxolan-2-yl)-N-[(2-methoxyethoxy)methyl]- 254744-50-8P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-2'-(1,3-dioxolan-2-yl)-4'-formyl-N-[(2-methoxyethoxy)methyl]- 254744-51-9P, [1,1'-Biphenyl]-2-sulfonamide, 4'-(bromomethyl)-N-(3,4-dimethyl-5-isoxazolyl)-2'-(1,3-dioxolan-2-yl)-N-[(2-methoxyethoxy)methyl]- 254744-52-0P 254744-53-1P, Benzaldehyde, 4-bromo-3-(1,3-dioxolan-2-yl)- 254744-54-2P, 1,3-Dioxolane, 2-[2-bromo-5-(bromomethyl)phenyl]- 254744-55-3P, 1,3-Diazaspiro[4.4]non-1-en-4-one, 3-[[4-bromo-3-(1,3-dioxolan-2-yl)phenyl]methyl]-2-butyl- 254744-56-4P 254744-58-6P 254744-60-0P 254744-63-3P 254744-65-5P 254744-68-8P 254744-70-2P 254744-73-5P, 1,2,4-Oxadiazole-5-methanamine, 3-methyl-.alpha.-(1-methylethyl)-, (.alpha.S)- 254744-78-0P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-4'-[[[(1S)-2-methyl-1-(3-methyl-1,2,4-oxadiazol-5-yl)propyl]amino]methyl]- 254744-81-5P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-2'-[(3,3-dimethyl-2-oxo-1-pyrrolidinyl)methyl]-4'-(hydroxymethyl)-N-[(2-methoxyethoxy)methyl]- 254744-84-8P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-2'-[(3,3-dimethyl-2-oxo-1-pyrrolidinyl)methyl]-4'-[(2-ethyl-5,7-dimethyl-3H-imidazo[4,5-b]pyridin-3-yl)methyl]-N-[(2-methoxyethoxy)methyl]- 254744-86-0P, Cyclopentanecarboxylic acid, 1-[(3-methoxy-1-oxopropyl)amino]-, methyl ester 254744-87-1P, Cyclopentanecarboxylic acid, 1-[(3-methoxy-1-oxopropyl)amino]- 254744-90-6P, Cyclopentanecarboxamide, 1-[(3-methoxy-1-oxopropyl)amino]- 254744-91-7P, 1,3-Diazaspiro[4.4]non-1-en-4-one, 2-(2-methoxyethyl)- 254744-95-1P, Cyclopentanecarboxylic acid, 1-[(ethoxyacetyl)amino]-, methyl ester 254744-98-4P, 1,3-Diazaspiro[4.4]non-1-en-4-one, 2-(ethoxymethyl)- 254745-00-1P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-2'-formyl-N-[(2-methoxyethoxy)methyl]-4'-[(methylsulfonyl)oxy]- 254745-03-4P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-4'-[(2-ethyl-5,7-dimethyl-3H-imidazo[4,5-b]pyridin-3-yl)methyl]-2'-formyl-N-[(2-methoxyethoxy)methyl]- 254745-06-7P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-4'-[(2-ethyl-5,7-dimethyl-3H-imidazo[4,5-b]pyridin-3-yl)methyl]-N-[(2-methoxyethoxy)methyl]-2'-[(2-oxo-1-pyrrolidinyl)methyl]- 254745-08-9P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-4'-[(2-ethyl-5,7-dimethyl-3H-imidazo[4,5-b]pyridin-3-yl)methyl]-N-[(2-methoxyethoxy)methyl]-2'-[(3-methyl-2-oxo-1-imidazolidinyl)methyl]- 254745-12-5P, Benzenesulfonamide, 2-bromo-N-(3-methyl-5-isoxazolyl)- 254745-14-7P, Benzenesulfonamide, 2-bromo-N-(3-methyl-5-isoxazolyl)-N-[[2-[(trimethylsilyl)oxy]ethoxy]methyl]- 254745-19-2P, [1,1'-Biphenyl]-2-sulfonamide, 4'-formyl-N-(3-methyl-5-isoxazolyl)-N-[[2-[(trimethylsilyl)oxy]ethoxy]methyl]- 254745-23-8P, Butanamide, N,3-dimethyl-2-[[[2'-[[(3-methyl-5-isoxazolyl)[[2-[(trimethylsilyl)oxy]ethoxy]methyl]amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]amino]-, (2S)- 254745-28-3P, Pentanamide, N-[[2'-[[(3-methyl-5-isoxazolyl)[[2-[(trimethylsilyl)oxy]ethoxy]methyl]amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-N-[(1S)-2-methyl-1-[(methylamino)carbonyl]propyl]- 254745-31-8P, Benzonitrile, 4-bromo-3-(1-propenyl)- 254745-36-3P, Benzonitrile, 4-bromo-3-propyl- 254745-39-6P, Benzaldehyde, 4-bromo-3-propyl- 254745-42-1P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-4'-formyl-N-[(2-methoxyethoxy)methyl]-2'-propyl- 254745-43-2P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-4'-(hydroxymethyl)-N-[(2-methoxyethoxy)methyl]-2'-propyl- 254745-45-4P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-N-[(2-methoxyethoxy)methyl]-4'-[[(methylsulfonyl)oxy]methyl]-2'-propyl- 254745-46-5P 254745-48-7P, Benzoic acid, 2-[[(4-bromophenyl)methyl]amino]-3-nitro-, methyl ester 254745-49-8P, Benzoic acid, 2-[[[2'-[[(3,4-dimethyl-5-isoxazolyl)[[2-

[(trimethylsilyl)oxy]ethoxy]methyl]amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]amino]-3-nitro-, methyl ester 254745-50-1P, Benzoic acid, 3-amino-2-[[[2'-[[(3,4-dimethyl-5-isoxazolyl)[[2-[(trimethylsilyl)oxy]ethoxy]methyl]amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]amino]-, methyl ester 254745-51-2P, 1H-Benzimidazole-7-carboxylic acid, 1-[[2'-[[(3,4-dimethyl-5-isoxazolyl)[[2-[(trimethylsilyl)oxy]ethoxy]methyl]amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-2-ethoxy-, methyl ester 254745-52-3P, Benzenemethanamine, 4-bromo-3-(1,3-dioxolan-2-yl)- 254745-53-4P, Benzoic acid, 2-[[[4-bromo-3-(1,3-dioxolan-2-yl)phenyl]methyl]amino]-3-nitro-, methyl ester 254745-54-5P, Benzoic acid, 2-[[[2'-[[(3,4-dimethyl-5-isoxazolyl)[[2-[(trimethylsilyl)oxy]ethoxy]methyl]amino]sulfonyl]-2-formyl[1,1'-biphenyl]-4-yl]methyl]amino]-3-nitro-, methyl ester 254745-55-6P, Benzoic acid, 2-[[[2'-[[(3,4-dimethyl-5-isoxazolyl)[[2-[(trimethylsilyl)oxy]ethoxy]methyl]amino]sulfonyl]-2-[(3,3-dimethyl-2-oxo-1-pyrrolidinyl)methyl][1,1'-biphenyl]-4-yl]methyl]amino]-3-nitro-, methyl ester 254745-57-8P, Benzoic acid, 3-amino-2-[[[2'-[[(3,4-dimethyl-5-isoxazolyl)[[2-[(trimethylsilyl)oxy]ethoxy]methyl]amino]sulfonyl]-2-[(3,3-dimethyl-2-oxo-1-pyrrolidinyl)methyl][1,1'-biphenyl]-4-yl]methyl]amino]-, methyl ester 254745-58-9P, 1H-Benzimidazole-7-carboxylic acid, 1-[[2'-[[(3,4-dimethyl-5-isoxazolyl)[[2-[(trimethylsilyl)oxy]ethoxy]methyl]amino]sulfonyl]-2-[(3,3-dimethyl-2-oxo-1-pyrrolidinyl)methyl][1,1'-biphenyl]-4-yl]methyl]-2-ethoxy-, methyl ester 254745-60-3P, Quinoline, 4-[(4-bromophenyl)methoxy]-2-ethyl- 254745-61-4P, [1,1'-Biphenyl]-2-sulfonamide, N-(1,1-dimethylethyl)-4'-[[(2-ethyl-4-quinolinyl)oxy]methyl]- 254745-62-5P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[[(2-ethyl-4-quinolinyl)oxy]methyl]- 254745-64-7P, [1,1'-Biphenyl]-2-sulfonic acid, 4'-[[(2-ethyl-4-quinolinyl)oxy]methyl]- 254745-66-9P, Ethanone, 1-(5-chloro-2-propyl-1H-imidazol-4-yl)- 254745-68-1P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(5-acetyl-4-chloro-2-propyl-1H-imidazol-1-yl)methyl]-N-(3,4-dimethyl-5-isoxazolyl)-N-[[2-[(trimethylsilyl)oxy]ethoxy]methyl]- 254745-70-5P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(4-chloro-5-formyl-2-propyl-1H-imidazol-1-yl)methyl]-N-(3,4-dimethyl-5-isoxazolyl)-N-[[2-[(trimethylsilyl)oxy]ethoxy]methyl]- 254745-72-7P, 1H-Imidazole-5-carboxylic acid, 4-chloro-1-[[2'-[[(3,4-dimethyl-5-isoxazolyl)[[2-[(trimethylsilyl)oxy]ethoxy]methyl]amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-2-propyl- 254745-73-8P, 1H-Imidazole-5-carboxylic acid, 4-chloro-1-[[2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-2-propyl- 254745-76-1P, 1H-Imidazole-5-carboxylic acid, 1-[[2'-[[(3,4-dimethyl-5-isoxazolyl)[(2-methoxyethoxy)methyl]amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-4-ethyl-2-propyl-, ethyl ester 254745-77-2P, 1H-Imidazole-5-carboxylic acid, 1-[[2'-[[(3,4-dimethyl-5-isoxazolyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]methyl]-4-ethyl-2-propyl- 254745-78-3P 254745-79-4P 254745-80-7P 254745-81-8P 254745-82-9P, Benzenesulfonamide, 2-bromo-N-(3-methoxy-5-methylpyrazinyl)- 254745-83-0P, Benzenesulfonamide, 2-bromo-N-(3-methoxy-5-methylpyrazinyl)-N-[[2-[(trimethylsilyl)oxy]ethoxy]methyl]- 254745-84-1P 254745-85-2P, [1,1'-Biphenyl]-2-sulfonamide, 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-2'-formyl-N-(3-methoxy-5-methylpyrazinyl)- 254745-86-3P, Benzenesulfonamide, 2-bromo-N-[(2-methoxyethoxy)methyl]-N-(3-methyl-5-isoxazolyl)- 254745-87-4P, Boronic acid, [2-[[[(2-methoxyethoxy)methyl](3-methyl-5-isoxazolyl)amino]sulfonyl]phenyl]- 254745-88-5P 254745-89-6P 254745-90-9P 254745-91-0P, Benzene, 4-(dimethoxymethyl)-1-methoxy-2-(3,3,3-trifluoropropyl)- 254745-92-1P, Benzaldehyde, 4-methoxy-3-(3,3,3-trifluoropropyl)- 254745-93-2P, Benzaldehyde, 4-hydroxy-3-(3,3,3-trifluoropropyl)- 254745-94-3P, Methanesulfonic acid, trifluoro-, 4-formyl-2-(3,3,3-trifluoropropyl)phenyl ester 254745-95-4P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-4'-formyl-2'-(3,3,3-trifluoropropyl)-N-[[2-[(trimethylsilyl)oxy]ethoxy]methyl]- 254745-96-5P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-4'-(hydroxymethyl)-2'-(3,3,3-trifluoropropyl)-N-[[2-[(trimethylsilyl)oxy]ethoxy]methyl]- 254745-97-6P

254745-98-7P, Benzoic acid, 3-(2-propenyl)-4-[[(trifluoromethyl)sulfonyl]oxy]-, methyl ester 254745-99-8P, Benzoic acid, 3-(3-hydroxypropyl)-4-[[(trifluoromethyl)sulfonyl]oxy]-, methyl ester 254746-00-4P, [1,1'-Biphenyl]-4-carboxylic acid, 2'-[[(3,4-dimethyl-5-isoxazolyl)[[2-[(trimethylsilyl)oxy]ethoxy]methyl]amino]sulfonyl]-2-(3-hydroxypropyl)-, methyl ester 254746-01-5P, [1,1'-Biphenyl]-4-carboxylic acid, 2'-[[(3,4-dimethyl-5-isoxazolyl)[[2-[(trimethylsilyl)oxy]ethoxy]methyl]amino]sulfonyl]-2-(3-fluoropropyl)-, methyl ester 254746-03-7P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-2'-(3-fluoropropyl)-4'-(hydroxymethyl)-N-[[2-[(trimethylsilyl)oxy]ethoxy]methyl]- 254746-04-8P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-2'-(3-fluoropropyl)-4'-[[(methylsulfonyl)oxy]methyl]-N-[[2-[(trimethylsilyl)oxy]ethoxy]methyl]- 254746-06-0P 254746-07-1P, Methanesulfonic acid, trifluoro-, 2-acetyl-4-bromophenyl ester 254746-08-2P, Methanesulfonic acid, trifluoro-, 4-bromo-2-(1,1-difluoroethyl)phenyl ester 254746-09-3P, Methanesulfonic acid, trifluoro-, 2-(1,1-difluoroethyl)-4-formylphenyl ester 254746-10-6P, [1,1'-Biphenyl]-2-sulfonamide, 2'-(1,1-difluoroethyl)-N-(3,4-dimethyl-5-isoxazolyl)-4'-formyl-N-[[2-[(trimethylsilyl)oxy]ethoxy]methyl]- 254746-11-7P, [1,1'-Biphenyl]-2-sulfonamide, 2'-(1,1-difluoroethyl)-N-(3,4-dimethyl-5-isoxazolyl)-4'-(hydroxymethyl)-N-[[2-[(trimethylsilyl)oxy]ethoxy]methyl]- 254746-12-8P, [1,1'-Biphenyl]-2-sulfonamide, 2'-(1,1-difluoroethyl)-N-(3,4-dimethyl-5-isoxazolyl)-4'-[[(methylsulfonyl)oxy]methyl]-N-[[2-[(trimethylsilyl)oxy]ethoxy]methyl]- 254746-13-9P 254746-14-0P, Benzoic acid, 4-bromo-3-(2,2,2-trifluoroethyl)-, methyl ester 254746-15-1P, [1,1'-Biphenyl]-4-carboxylic acid, 2'-[[(3,4-dimethyl-5-isoxazolyl)[[2-[(trimethylsilyl)oxy]ethoxy]methyl]amino]sulfonyl]-2-(2,2,2-trifluoroethyl)-, methyl ester 254746-16-2P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-4'-(hydroxymethyl)-2'-(2,2,2-trifluoroethyl)-N-[[2-[(trimethylsilyl)oxy]ethoxy]methyl]- 254746-18-4P 254746-19-5P, Benzene, 1-bromo-4-methyl-2-(2-methylpropoxy)- 254746-20-8P, Benzene, 1-bromo-4-(bromomethyl)-2-(2-methylpropoxy)- 254746-21-9P, 1,3-Diazaspiro[4.4]non-1-en-4-one, 3-[[4-bromo-3-(2-methylpropoxy)phenyl]methyl]-2-butyl- 254746-22-0P 254746-23-1P, Benzene, 1-bromo-2-(2-methoxyethoxy)-4-methyl- 254746-24-2P, Benzene, 1-bromo-4-(bromomethyl)-2-(2-methoxyethoxy)- 254746-25-3P, 1,3-Diazaspiro[4.4]non-1-en-4-one, 3-[[4-bromo-3-(2-methoxyethoxy)phenyl]methyl]-2-butyl- 254746-26-4P 254746-27-5P, Benzonitrile, 4-bromo-3-(1-butenyl)- 254746-28-6P, Benzonitrile, 4-bromo-3-butyl- 254746-29-7P, Benzaldehyde, 4-bromo-3-butyl- 254746-30-0P, [1,1'-Biphenyl]-2-sulfonamide, 2'-butyl-N-(3,4-dimethyl-5-isoxazolyl)-4'-(hydroxymethyl)-N-[[2-[(trimethylsilyl)oxy]ethoxy]methyl]- 254746-31-1P, [1,1'-Biphenyl]-2-sulfonamide, 2'-butyl-N-(3,4-dimethyl-5-isoxazolyl)-4'-[[(methylsulfonyl)oxy]methyl]-N-[[2-[(trimethylsilyl)oxy]ethoxy]methyl]- 254746-32-2P 254746-33-3P, Boronic acid, [2-[[(3-methyl-5-isoxazolyl)[[2-[(trimethylsilyl)oxy]ethoxy]methyl]amino]sulfonyl]phenyl]- 254746-34-4P, [1,1'-Biphenyl]-2-sulfonamide, 4'-formyl-N-(3-methyl-5-isoxazolyl)-2'-(trifluoromethyl)-N-[[2-[(trimethylsilyl)oxy]ethoxy]methyl]- 254746-35-5P, [1,1'-Biphenyl]-2-sulfonamide, 4'-(hydroxymethyl)-N-(3-methyl-5-isoxazolyl)-2'-(trifluoromethyl)-N-[[2-[(trimethylsilyl)oxy]ethoxy]methyl]- 254746-36-6P 254746-37-7P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-4'-(hydroxymethyl)-N-[(2-methoxyethoxy)methyl]-2'-[(methoxymethylamino)methyl]- 254746-38-8P, [1,1'-Biphenyl]-2-sulfonamide, 4'-(bromomethyl)-N-(3,4-dimethyl-5-isoxazolyl)-N-[(2-methoxyethoxy)methyl]-2'-[(methoxymethylamino)methyl]- 254746-39-9P 254746-40-2P, Benzoic acid, 4-bromo-3-(hydroxymethyl)-, methyl ester 254746-41-3P, Benzoic acid, 3-[(acetyloxy)methyl]-4-bromo-, methyl ester 254746-42-4P, Benzoic acid, 4-bromo-3-[[(tetrahydro-2H-pyran-2-yl)oxy]methyl]-, methyl ester 254746-43-5P, [1,1'-Biphenyl]-4-carboxylic acid, 2'-[[(3,4-dimethyl-5-isoxazolyl)[[2-[(trimethylsilyl)oxy]ethoxy]meth

yl]amino]sulfonyl]-2-[[(tetrahydro-2H-pyran-2-yl)oxy]methyl]-, methyl ester 254746-44-6P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-4'-(hydroxymethyl)-2'-[[(tetrahydro-2H-pyran-2-yl)oxy]methyl]-N-[[2-[(trimethylsilyl)oxy]ethoxy]methyl]- 254746-45-7P 254746-46-8P 254746-47-9P 254746-48-0P, Benzoic acid, 3-(2-hydroxyethyl)-4-[[(trifluoromethyl)sulfonyl]oxy]-, methyl ester 254746-49-1P, [1,1'-Biphenyl]-4-carboxylic acid, 2'-[[(3,4-dimethyl-5-isoxazolyl)[[2-[(trimethylsilyl)oxy]ethoxy]methyl]amino]sulfonyl]-2-(2-hydroxyethyl)-, methyl ester 254746-50-4P, [1,1'-Biphenyl]-4-carboxylic acid, 2'-[[(3,4-dimethyl-5-isoxazolyl)[[2-[(trimethylsilyl)oxy]ethoxy]methyl]amino]sulfonyl]-2-(2-fluoroethyl)-, methyl ester 254746-51-5P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-2'-(2-fluoroethyl)-4'-(hydroxymethyl)-N-[[2-[(trimethylsilyl)oxy]ethoxy]methyl]- 254746-52-6P 254746-53-7P

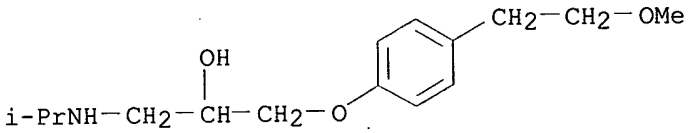
, [1,1'-Biphenyl]-4-carboxylic acid, 2'-[[(3,4-dimethyl-5-isoxazolyl)[[2-[(trimethylsilyl)oxy]ethoxy]methyl]amino]sulfonyl]-2-[2-[(tetrahydro-2H-pyran-2-yl)oxy]ethyl]-, methyl ester 254746-54-8P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-4'-(hydroxymethyl)-2'-[2-[(tetrahydro-2H-pyran-2-yl)oxy]ethyl]-N-[[2-[(trimethylsilyl)oxy]ethoxy]methyl]- 254746-55-9P, Benzonitrile, 4-bromo-3-(3-methyl-1-butenyl)- 254746-56-0P, Benzonitrile, 4-bromo-3-(3-methylbutyl)- 254746-57-1P, Benzaldehyde, 4-bromo-3-(3-methylbutyl)- 254746-58-2P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-4'-(hydroxymethyl)-N-[(2-methoxyethoxy)methyl]-2'-(3-methylbutyl)- 254746-59-3P, [1,1'-Biphenyl]-2-sulfonamide, 4'-(bromomethyl)-N-(3,4-dimethyl-5-isoxazolyl)-N-[(2-methoxyethoxy)methyl]-2'-(3-methylbutyl)- 254746-60-6P, Benzonitrile, 4-[(2-methyl-2-propenyl)oxy]- 254746-61-7P, Benzonitrile, 4-hydroxy-3-(2-methyl-2-propenyl)- 254746-62-8P, Benzonitrile, 4-hydroxy-3-(2-methylpropyl)- 254746-63-9P, Benzaldehyde, 4-hydroxy-3-(2-methylpropyl)- 254746-64-0P, Methanesulfonic acid, trifluoro-, 4-formyl-2-(2-methylpropyl)phenyl ester 254746-65-1P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-4'-formyl-N-[(2-methoxyethoxy)methyl]-2'-(2-methylpropyl)- 254746-66-2P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-4'-(hydroxymethyl)-N-[(2-methoxyethoxy)methyl]-2'-(2-methylpropyl)- 254746-67-3P, [1,1'-Biphenyl]-2-sulfonamide, 4'-(bromomethyl)-N-(3,4-dimethyl-5-isoxazolyl)-N-[(2-methoxyethoxy)methyl]-2'-(2-methylpropyl)- 254746-68-4P 254746-69-5P, Cyclopentanecarboxylic acid, 1-[(3,3-difluoro-1-oxobutyl)amino]-, methyl ester 254746-70-8P, 1,3-Diazaspiro[4.4]non-1-en-4-one, 2-(3,3-difluorobutyl)- 254746-71-9P, [1,1'-Biphenyl]-2-sulfonamide, N-(3,4-dimethyl-5-isoxazolyl)-4'-[[(3-methoxy-2,6-dimethyl-4-pyridinyl)oxy]methyl]-2'-(3,3,3-trifluoropropyl)-N-[[2-[(trimethylsilyl)oxy]ethoxy]methyl]- 254746-72-0P, Benzoic acid, 4-bromo-3-[(1,1-dimethylethoxy)methyl]-, methyl ester 254746-73-1P, [1,1'-Biphenyl]-4-carboxylic acid, 2-[(1,1-dimethylethoxy)methyl]-2'-[[(3,4-dimethyl-5-isoxazolyl)[[2-[(trimethylsilyl)oxy]ethoxy]methyl]amino]sulfonyl]-, methyl ester 254746-74-2P, [1,1'-Biphenyl]-2-sulfonamide, 2'-[(1,1-dimethylethoxy)methyl]-N-(3,4-dimethyl-5-isoxazolyl)-4'-(hydroxymethyl)-N-[[2-[(trimethylsilyl)oxy]ethoxy]methyl]- 254746-75-3P, [1,1'-Biphenyl]-2-sulfonamide, 4'-(bromomethyl)-2'-[(1,1-dimethylethoxy)methyl]-N-(3,4-dimethyl-5-isoxazolyl)-N-[[2-[(trimethylsilyl)oxy]ethoxy]methyl]- 254746-76-4P 254746-82-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of N-isoxazolyl biphenylsulfonamides and related compds. as dual angiotensin II and endothelin receptor antagonists)

IT 50-78-2, Aspirin 52-01-7, Spironolactone 10238-21-8, Glyburide **51384-51-1, Metoprolol** 55142-85-3, Ticlopidine 72956-09-3, Carvedilol 75330-75-5, Lovastatin 79902-63-9, Simvastatin 81093-37-0, Pravastatin **107724-20-9, Eplerenone** 113665-84-2, Clopidogrel 134523-00-5, Atorvastatin 147098-20-2, Zd-4522 147526-32-7, NK 104 150322-43-3, Cs-747
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(prepn. of N-isoxazolyl biphenylsulfonamides and related compds. as dual angiotensin II and endothelin receptor antagonists)

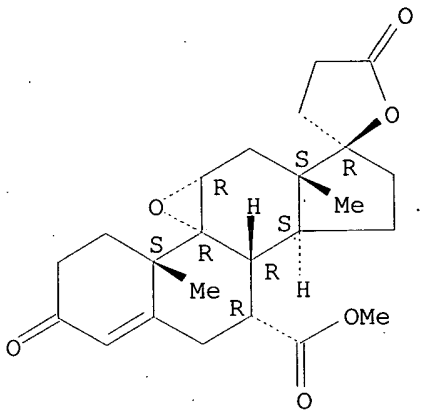
IT **51384-51-1, Metoprolol 107724-20-9, Eplerenone**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of N-isoxazolyl biphenylsulfonamides and related compds. as dual angiotensin II and endothelin receptor antagonists)

RN 51384-51-1 HCAPLUS
CN 2-Propanol, 1-[4-(2-methoxyethyl)phenoxy]-3-[(1-methylethyl)amino]- (9CI) (CA INDEX NAME)



RN 107724-20-9 HCAPLUS
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, .gamma.-lactone, methyl ester, (7.alpha.,11.alpha.,17.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L68 ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2003 ACS
AN 2002:107159 HCAPLUS
DN 136:172753
TI Epoxy-steroidal aldosterone antagonist and beta-adrenergic antagonist combination therapy for treatment of congestive heart failure
IN **Alexander, John C.; Schuh, Joseph R.**
PA Pharmacia Corporation, USA
SO PCT Int. Appl., 190 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K045-06
ICS A61K031-58; A61P009-00; A61K031-58; A61K031-135; A61K045-06; A61K031-58
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1, 2
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI WO 2002009760 A2 20020207 WO 2001-US23670 20010727 <--
WO 2002009760 A3 20030123
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
US 2002123485 A1 20020905 US 2001-917403 20010727 <--
EP 1303306 A2 20030423 EP 2001-957290 20010727 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

PRAI US 2000-221365P P 20000727 <--
WO 2001-US23670 W 20010727 <--

AB A combination therapy comprising a therapeutically-effective amt. of an epoxy-steroidal aldosterone receptor antagonist and a therapeutically-effective amt. of a beta-adrenergic antagonist is described for treatment of circulatory disorders, including cardiovascular disorders such as hypertension, congestive heart failure, cirrhosis and ascites. Preferred beta-adrenergic antagonists are those compds. having high potency and bioavailability. Preferred epoxy-steroidal aldosterone receptor antagonists are 20-spiroxane steroidal compds. characterized by the presence of a 9.alpha., 11.alpha.-substituted epoxy moiety. A preferred combination therapy includes the beta-adrenergic antagonist **metoprolol** succinate and the aldosterone receptor antagonist epoxymexrenone. Crystal forms of **eplerenone** were prepd. as well as the Me Et ketone solvate.

ST epoxy steroid aldosterone antagonist beta adrenergic antagonist; congestive heart failure treatment compn

IT Cardiovascular agents
Crystal morphology
Crystallization
Human
(epoxy-steroidal aldosterone antagonist and beta-adrenergic antagonist combination therapy for treatment of congestive heart failure)

IT Mineralocorticoid receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(epoxy-steroidal aldosterone antagonist and beta-adrenergic antagonist combination therapy for treatment of congestive heart failure)

IT Steroids, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(epoxy-steroidal aldosterone antagonist and beta-adrenergic antagonist combination therapy for treatment of congestive heart failure)

IT Heart, disease
(failure; epoxy-steroidal aldosterone antagonist and beta-adrenergic antagonist combination therapy for treatment of congestive heart failure)

IT Adrenoceptor antagonists
(.beta.-; epoxy-steroidal aldosterone antagonist and beta-adrenergic antagonist combination therapy for treatment of congestive heart failure)

IT 170684-14-7, UK 1745
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(UK 1745; epoxy-steroidal aldosterone antagonist and beta-adrenergic antagonist combination therapy for treatment of congestive heart failure)

IT 52-39-1, Aldosterone
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antagonists; epoxy-steroidal aldosterone antagonist and beta-adrenergic antagonist combination therapy for treatment of

congestive heart failure)

IT **395665-44-8P 395665-46-0P**
RL: BYP (Byproduct); PREP (Preparation)
(epoxy-steroidal aldosterone antagonist and beta-adrenergic antagonist combination therapy for treatment of congestive heart failure)

IT **344449-96-3**
RL: FMU (Formation, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); FORM (Formation, nonpreparative); USES (Uses)
(epoxy-steroidal aldosterone antagonist and beta-adrenergic antagonist combination therapy for treatment of congestive heart failure)

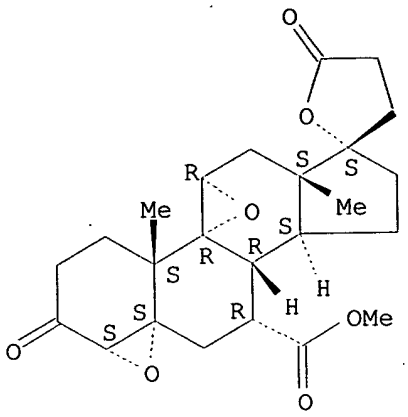
IT **107724-20-9, Eplerenone**
RL: PAC (Pharmacological activity); PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(epoxy-steroidal aldosterone antagonist and beta-adrenergic antagonist combination therapy for treatment of congestive heart failure)

IT 52-01-7, Spironolactone 525-66-6, Propranolol 3930-20-9, Sotalol
6452-71-7, Oxprenolol 7413-36-7, Nifenalol 13523-86-9, Pindolol
13655-52-2, Alprenolol 22664-55-7, Metipranolol 23694-81-7, Mepindolol
26839-75-8, Timolol 29122-68-7, Atenolol 34915-68-9, Bunitrolol
36894-69-6, Labetalol 37517-30-9, Acebutolol 38363-40-5, Penbutolol
39552-01-7, Befunolol 39563-28-5, Cloranolol 42200-33-9, Nadolol
47141-42-4, Levobunolol **51384-51-1, Metoprolol**
51781-06-7, Carteolol 56980-93-9, Celiprolol 57460-41-0, Talinolol
57775-29-8, Carazolol 58409-59-9, Bucumolol 58930-32-8, Butofilolol
59170-23-9, Bevantolol 60607-68-3, Indenolol 62658-63-3, Bopindolol
63659-18-7, Betaxolol 66722-44-9, Bisoprolol 66848-46-2, Viskenit
68377-92-4, Arotinolol 71119-11-4, Bucindolol 72956-09-3, Carvedilol
77164-20-6, Levomoprolol 81147-92-4, Esmolol 81447-80-5, Diprafenone
81486-22-8, Nipradilol 81801-12-9, Xamoterol 83688-84-0, Tertatolol
85136-71-6, Tilisolol 85320-68-9, Amosulalol 93379-54-5, S-Atenolol
98418-47-4, Toprol xl 102203-23-6, Acc 9369 114856-47-2, TZC-5665
115609-61-5, L-653328 118457-14-0, Nebivolol 125279-79-0, Ersentilide
132017-03-9, SR 58894A 133242-30-5, Landiolol 153192-22-4, YM-430
153601-03-7, Capsinolol 165337-66-6, LM-2616 174689-39-5, SR-59230A
188564-74-1, Fr-172516 207922-70-1 264134-39-6, SB-226552
395665-48-2 395665-50-6 395665-52-8
395665-54-0 395665-56-2 395665-58-4
395665-60-8 395665-62-0 395665-64-2
395665-66-4 395665-68-6 396654-09-4 396712-03-1, AMO 140 396712-06-4, ISV 208 396712-07-5, PharmaProjects 5279
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(epoxy-steroidal aldosterone antagonist and beta-adrenergic antagonist combination therapy for treatment of congestive heart failure)

IT **395665-44-8P 395665-46-0P**
RL: BYP (Byproduct); PREP (Preparation)
(epoxy-steroidal aldosterone antagonist and beta-adrenergic antagonist combination therapy for treatment of congestive heart failure)

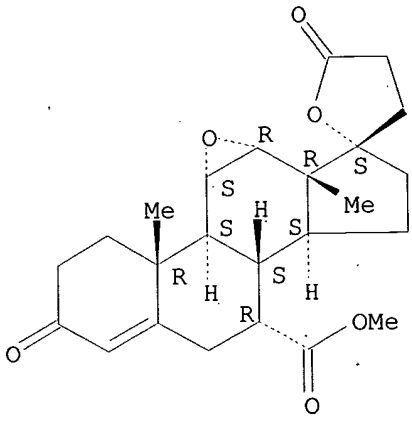
RN 395665-44-8 HCAPLUS
CN Pregnane-7,21-dicarboxylic acid, 4,5:9,11-diepoxy-17-hydroxy-3-oxo-, .gamma.-lactone, methyl ester, (4.alpha.,5.alpha.,7.alpha.,11.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 395665-46-0 HCAPLUS
CN Pregn-4-ene-7,21-dicarboxylic acid, 11,12-epoxy-17-hydroxy-3-oxo-, .gamma.-lactone, methyl ester, (7.alpha.,11.alpha.,12.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

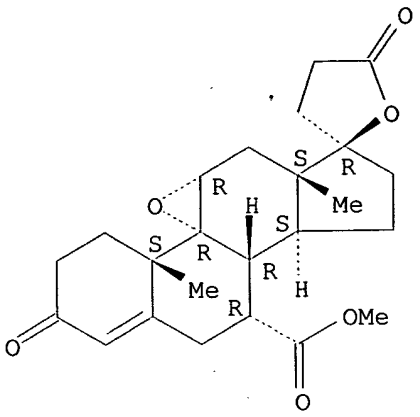


IT **344449-96-3**
RL: FMU (Formation, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); FORM (Formation, nonpreparative); USES (Uses)
(epoxy-steroidal aldosterone antagonist and beta-adrenergic antagonist combination therapy for treatment of congestive heart failure)
RN 344449-96-3 HCAPLUS
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, .gamma.-lactone, methyl ester, (7.alpha.,11.alpha.,17.alpha.)-, compd. with 2-butanone (9CI) (CA INDEX NAME)

CM 1

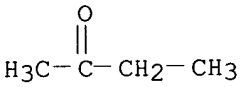
CRN 107724-20-9
CMF C24 H30 O6

Absolute stereochemistry.



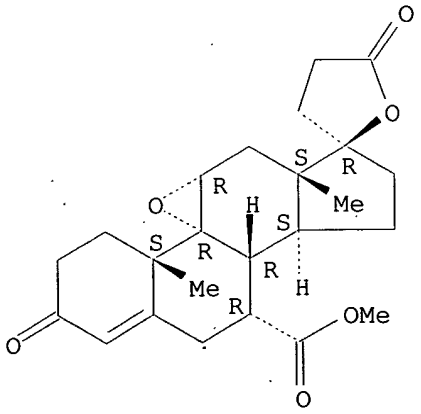
CM 2

CRN 78-93-3
CMF C4 H8 O



IT **107724-20-9, Eplerenone**
RL: PAC (Pharmacological activity); PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(epoxy-steroidal aldosterone antagonist and beta-adrenergic antagonist combination therapy for treatment of congestive heart failure)
RN 107724-20-9 HCAPLUS
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, .gamma.-lactone, methyl ester, (7.alpha.,11.alpha.,17.alpha.)- (9CI) (CA INDEX NAME)

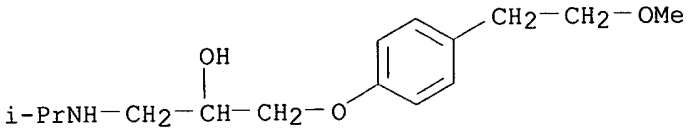
Absolute stereochemistry.



IT **51384-51-1, Metoprolol 395665-48-2**
395665-50-6 395665-52-8 395665-54-0
395665-56-2 395665-58-4 395665-60-8

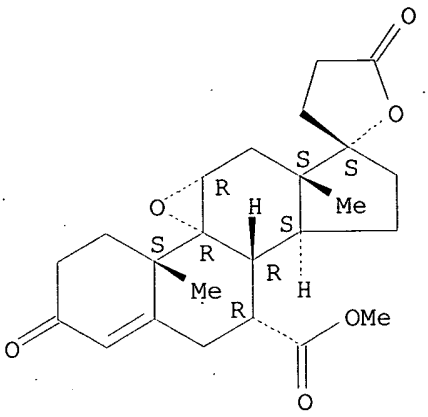
395665-62-0 395665-64-2 395665-66-4
395665-68-6
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(epoxy-steroidal aldosterone antagonist and beta-adrenergic antagonist combination therapy for treatment of congestive heart failure)

RN 51384-51-1 HCAPLUS
CN 2-Propanol, 1-[4-(2-methoxyethyl)phenoxy]-3-[(1-methylethyl)amino]- (9CI) (CA INDEX NAME)



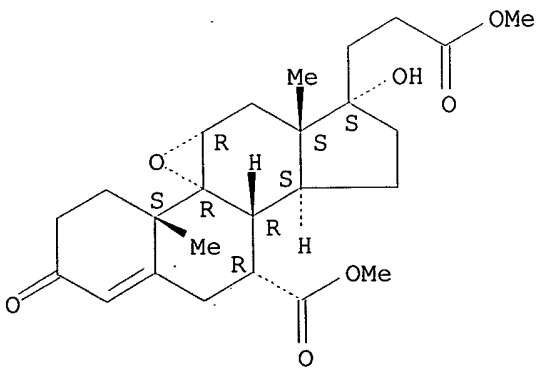
RN 395665-48-2 HCAPLUS
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, .gamma.-lactone, methyl ester, (7.alpha.,11.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 395665-50-6 HCAPLUS
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, dimethyl ester, (7.alpha.,11.alpha.)- (9CI) (CA INDEX NAME)

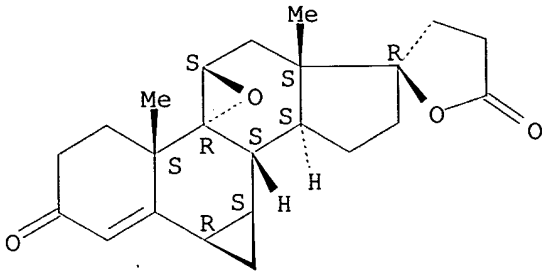
Absolute stereochemistry.



RN 395665-52-8 HCAPLUS

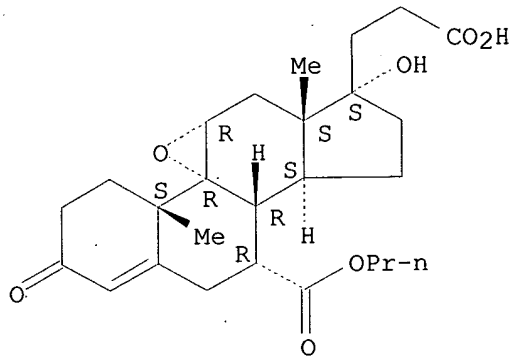
CN 3'H-Cyclopropa[6,7]pregna-4,6-diene-21-carboxylic acid, 9,11-epoxy-6,7-dihydro-17-hydroxy-3-oxo-, .gamma.-lactone, (6.alpha.,7.alpha.,11.beta.,17.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 395665-54-0 HCAPLUS
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, 7-propyl ester, monopotassium salt, (7.alpha.,11.alpha.)- (9CI) (CA INDEX NAME)

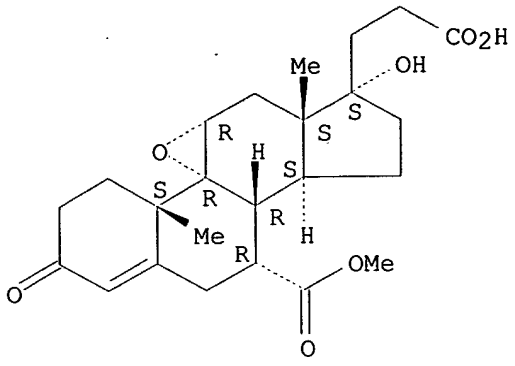
Absolute stereochemistry.



● K

RN 395665-56-2 HCAPLUS
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, 7-methyl ester, monopotassium salt, (7.alpha.,11.alpha.)- (9CI) (CA INDEX NAME)

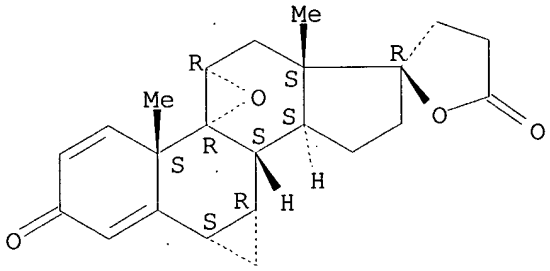
Absolute stereochemistry.



● K

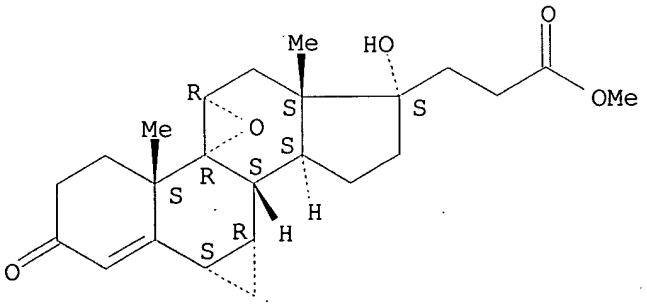
RN 395665-58-4 HCAPLUS
CN 3'H-Cyclopropa[6,7]pregna-1,4,6-triene-21-carboxylic acid, 9,11-epoxy-6,7-dihydro-17-hydroxy-3-oxo-, .gamma.-lactone, (6.beta.,7.beta.,11.alpha.,17.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



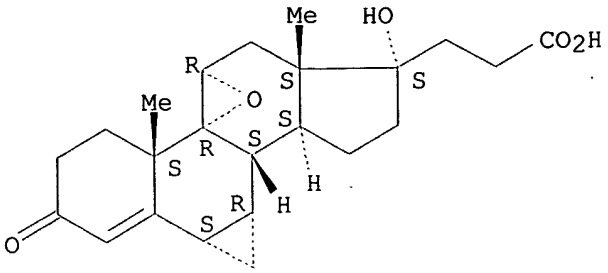
RN 395665-60-8 HCAPLUS
CN 3'H-Cyclopropa[6,7]pregna-4,6-diene-21-carboxylic acid, 9,11-epoxy-6,7-dihydro-17-hydroxy-3-oxo-, methyl ester, (6.beta.,7.beta.,11.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 395665-62-0 HCAPLUS
CN 3'H-Cyclopropa[6,7]pregna-4,6-diene-21-carboxylic acid, 9,11-epoxy-6,7-dihydro-17-hydroxy-3-oxo-, monopotassium salt, (6.beta.,7.beta.,11.alpha.)- (9CI) (CA INDEX NAME)

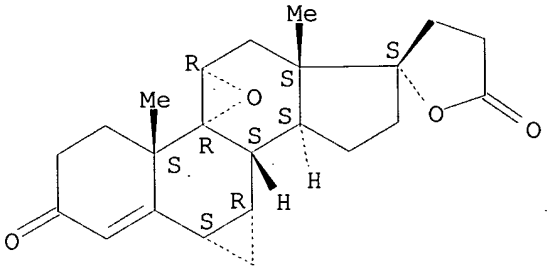
Absolute stereochemistry.



● K

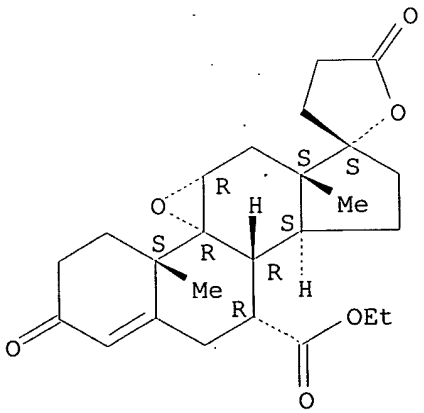
RN 395665-64-2 HCAPLUS
CN 3'H-Cyclopropa[6,7]pregna-4,6-diene-21-carboxylic acid, 9,11-epoxy-6,7-dihydro-17-hydroxy-3-oxo-, .gamma.-lactone, (6.beta.,7.beta.,11.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 395665-66-4 HCAPLUS
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, .gamma.-lactone, ethyl ester, (7.alpha.,11.alpha.)- (9CI) (CA INDEX NAME)

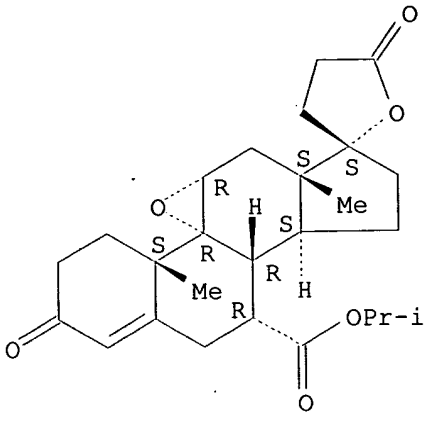
Absolute stereochemistry.



RN 395665-68-6 HCAPLUS
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,

.gamma.-lactone, 1-methylethyl ester, (7.alpha.,11.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L68 ANSWER 4 OF 4 HCAPLUS COPYRIGHT 2003 ACS
AN 2000:259979 HCAPLUS
DN 132:288794
TI Sympathetic nervous system activity-reducing agents for treatment of disease- or age-related weight loss and for enhancement of exercise performance
IN Anker, Stefan Dietmar; Coats, Andrew Justin Stewart
PA Imperial College Innovations Limited, UK
SO PCT Int. Appl., 72 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K031-00
CC 1-12 (Pharmacology)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000021509	A2	20000420	WO 1999-GB3302	19991015
	WO 2000021509	A3	20001109		
	W: JP, US				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	EP 1121111	A2	20010808	EP 1999-947762	19991015
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 2002527378	T2	20020827	JP 2000-575485	19991015
PRAI	GB 1998-22458	A	19981015		
	GB 1998-22459	A	19981015		
	GB 1999-17181	A	19990723		
	WO 1999-GB3302	W	19991015		

AB A method of treating wt. loss due to underlying disease in a patient, the method comprising administering to the patient an effective amt. of an agent which reduces sympathetic nervous system activity. A method of treating wt. loss due to underlying disease in a patient, the method comprising administering to the patient an effective amt. of any one or more of the following: a compd. which inhibits the effect of aldosterone such as an aldosterone antagonist; a chymase inhibitor; a cathepsin B inhibitor; a .beta. receptor blocker; an imidazoline receptor antagonist; a centrally acting .alpha. receptor antagonist; a peripherally acting .alpha. receptor antagonist; a ganglion blocking agent; a drug that has an

effect on cardiovascular reflexes and thereby reduces SNS activity such as an opiate; scopolamine; an endothelin receptor antagonist; and a xanthine oxidase inhibitor. The methods are particularly useful in treating cardiac cachexia. The sympathetic nervous system activity-reducing agents may also be used to treat wt. loss due to aging and to enhance exercise performance.

ST sympathetic agent disease related wt loss; age related wt loss sympathetic agent; exercise performance cardiac cachexia sympathetic agent

IT Anabolic agents
(anabolic growth factors; sympathetic nervous system activity-reducing agents for treatment of disease- or age-related wt. loss and for enhancement of exercise performance)

IT Angiotensin receptor antagonists
(angiotensin II; sympathetic nervous system activity-reducing agents for treatment of disease- or age-related wt. loss and for enhancement of exercise performance)

IT Endothelin receptors
Imidazoline receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antagonists; sympathetic nervous system activity-reducing agents for treatment of disease- or age-related wt. loss and for enhancement of exercise performance)

IT Reflex
(cardiovascular; sympathetic nervous system activity-reducing agents for treatment of disease- or age-related wt. loss and for enhancement of exercise performance)

IT Lung, disease
(chronic obstructive; sympathetic nervous system activity-reducing agents for treatment of disease- or age-related wt. loss and for enhancement of exercise performance)

IT Infection
(chronic; sympathetic nervous system activity-reducing agents for treatment of disease- or age-related wt. loss and for enhancement of exercise performance)

IT Muscle
(elec. stimulation of; sympathetic nervous system activity-reducing agents for treatment of disease- or age-related wt. loss and for enhancement of exercise performance)

IT Peptides, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(epoxysuccinyl; sympathetic nervous system activity-reducing agents for treatment of disease- or age-related wt. loss and for enhancement of exercise performance)

IT Heart, disease
Kidney, disease
(failure, chronic; sympathetic nervous system activity-reducing agents for treatment of disease- or age-related wt. loss and for enhancement of exercise performance)

IT Nervous system agents
(ganglionic blocking agents; sympathetic nervous system activity-reducing agents for treatment of disease- or age-related wt. loss and for enhancement of exercise performance)

IT Body weight
(loss; sympathetic nervous system activity-reducing agents for treatment of disease- or age-related wt. loss and for enhancement of exercise performance)

IT AIDS (disease)
Aging, animal
Cachexia
Cirrhosis
Disease, animal

Emphysema
Exercise
Heart, disease
Hypertension
Malnutrition
Neoplasm
Nervous system agents
(sympathetic nervous system activity-reducing agents for treatment of disease- or age-related wt. loss and for enhancement of exercise performance)

IT Opioids
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sympathetic nervous system activity-reducing agents for treatment of disease- or age-related wt. loss and for enhancement of exercise performance)

IT Nervous system
(sympathetic; sympathetic nervous system activity-reducing agents for treatment of disease- or age-related wt. loss and for enhancement of exercise performance)

IT Tumor necrosis factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(.alpha., antagonists; sympathetic nervous system activity-reducing agents for treatment of disease- or age-related wt. loss and for enhancement of exercise performance)

IT Adrenoceptor antagonists
(.alpha.-; sympathetic nervous system activity-reducing agents for treatment of disease- or age-related wt. loss and for enhancement of exercise performance)

IT Adrenoceptor antagonists
(.beta.-; sympathetic nervous system activity-reducing agents for treatment of disease- or age-related wt. loss and for enhancement of exercise performance)

IT 180384-56-9, Ro 61-1790
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Ro 61-1790; sympathetic nervous system activity-reducing agents for treatment of disease- or age-related wt. loss and for enhancement of exercise performance)

IT 188307-16-6, T 0201
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(T 0201; sympathetic nervous system activity-reducing agents for treatment of disease- or age-related wt. loss and for enhancement of exercise performance)

IT 52-39-1, Aldosterone
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(and aldosterone antagonists; sympathetic nervous system activity-reducing agents for treatment of disease- or age-related wt. loss and for enhancement of exercise performance)

IT 9002-17-9, Xanthine oxidase 9004-08-4, Cathepsin 9015-82-1, Angiotensin-converting enzyme 9047-22-7, Cathepsin B 97501-92-3, Chymase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; sympathetic nervous system activity-reducing agents for treatment of disease- or age-related wt. loss and for enhancement of exercise performance)

IT 9002-72-6, Growth hormone 67763-96-6, IGF-1
RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(sympathetic nervous system activity-reducing agents for treatment of disease- or age-related wt. loss and for enhancement of exercise performance)

IT 51-34-3, Scopolamine 52-01-7, Spironolactone 52-01-7D, Spironolactone, 15,16-methylene derivs. 57-27-2, Morphine, biological studies 60-26-4, Hexamethonium 60-30-0, Azamethonium 60-40-2, Mecamylamine 68-91-7 71-91-0, Tetraethylammonium bromide 100-33-4, Pentamidine 119-44-8, Xanthopterin 125-28-0, Dihydrocodeine 144-44-5, Pentolinium 315-30-0, Allopurinol 382-82-1 492-11-5, Leukopterin 497-23-4, 2(5H)-Furanone 525-66-6, Propranolol 546-48-5, Synapleg 555-30-6, .alpha.-Methyldopa 561-27-3, Diamorphine 968-93-4, Testolactone 971-60-8, Benzohexonium 1218-98-0, 7,8-Dihydroneopterin 2009-64-5, Neopterin 2365-25-5, Pentamethonium 2465-59-0, Oxypurinol 3613-69-2, Cypenam 3930-20-9, Sotalol 4138-96-9 4205-90-7, Clonidine 4844-10-4, Hexafluorenium 5472-41-3, 4-Amino-6-hydroxypyrazolo[3,4-d]pyrimidine 6452-71-7, Oxprenolol 7187-66-8, Trimetaphan 9087-70-1, Aprotinin 11096-26-7, Erythropoietin 13523-86-9, Pindolol 13655-52-2, Alprenolol 17528-72-2 19216-56-9, Prazosin 22150-76-1, Biopterin 22664-55-7, Metipranolol 26839-75-8, Timolol 29122-68-7, Atenolol 36894-69-6 37517-30-9, Acebutolol 38363-40-5, Penbutolol 42200-33-9, Nadolol 47141-42-4, Levobunolol **51384-51-1**, **Metoprolol** 51781-06-7, Carteolol 52485-79-7, Buprenorphine 54187-04-1, Rilmenidine 56980-93-9, Celiprolol 63590-64-7, Terazosin 63659-18-7, Betaxolol 66376-36-1, Alendronate 66722-44-9 67392-87-4, Dihydrospirorenone 71119-11-4, Bucindolol 72956-09-3, Carvedilol 74191-85-8, Doxazosin 74220-07-8, Spirorenone 75438-57-2, Moxonidine 76676-33-0, RU26752 76684-89-4, E 64c 81147-92-4, Esmolol 86102-31-0, Tissue inhibitor of matrix metalloproteinase 87952-98-5, Mespirenone 91448-99-6, Cystatin C 93519-21-2 95847-70-4, Ipsapirone 107544-29-6, Stefin A **107724-20-9**, **Eplerenone** 118457-14-0, Nebivolol 134448-10-5, CA-074 136553-74-7, WS 7338B 136553-81-6, BQ123 144602-02-8, IRL 1038 145380-08-1, RU40555 151039-33-7, PD 142893 156161-89-6, BQ-788 157659-79-5, SB 209670 162117-90-0, S 0139 162412-70-6, PD 156707 171714-84-4, LU135252 173189-01-0, IRL 3461 173937-91-2, ABT-627 204326-22-7, PD 164333 223756-43-2, A-216546 264276-89-3
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sympathetic nervous system activity-reducing agents for treatment of disease- or age-related wt. loss and for enhancement of exercise performance)

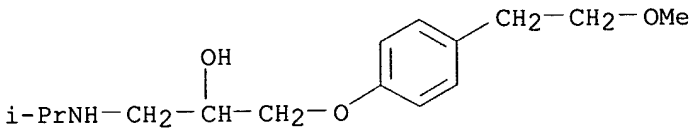
IT 75847-73-3, Enalapril 114798-26-4, Losartan
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sympathetic nervous system activity-reducing agents for treatment of disease- or age-related wt. loss and for enhancement of exercise performance)

IT 51-41-2, Noradrenaline 51-43-4, Epinephrine 11128-99-7, Angiotensin II 123626-67-5, Endothelin 1
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(sympathetic nervous system activity-reducing agents for treatment of disease- or age-related wt. loss and for enhancement of exercise performance)

IT **51384-51-1**, **Metoprolol** **107724-20-9**, **Eplerenone**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

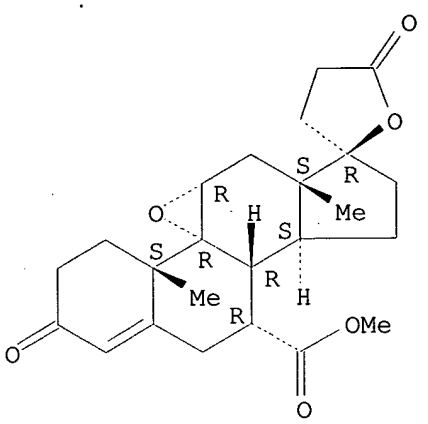
(sympathetic nervous system activity-reducing agents for treatment of disease- or age-related wt. loss and for enhancement of exercise performance)

RN 51384-51-1 HCAPLUS
CN 2-Propanol, 1-[4-(2-methoxyethyl)phenoxy]-3-[(1-methylethyl)amino]- (9CI) (CA INDEX NAME)



RN 107724-20-9 HCAPLUS
CN Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, .gamma.-lactone, methyl ester, (7.alpha.,11.alpha.,17.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



=> d his

(FILE 'HOME' ENTERED AT 15:17:42 ON 24 JUN 2003)
SET COST OFF

FILE 'REGISTRY' ENTERED AT 15:17:54 ON 24 JUN 2003
E METOPROLOL/CN
L1 1 S E3
SEL RN
L2 29 S E1/CRN
L3 17 S L2 NOT MXS/CI
L4 229 S C15H25NO3/MF AND 46.150.18/RID AND 1/NR
L5 17 S L4 AND 2 PROPANOL AND 2 METHOXYETHYL PHENOXY
L6 13 S L5 NOT (D OR T)/ELS
L7 7 S L6 AND 4
SEL RN
L8 14 S E2-E8/CRN NOT L2
L9 13 S L8 NOT MXS/CI
L10 7 S L9 NOT COMPD
L11 31 S L1,L3,L7,L10
L12 22 S L11 NOT (COMPD OR WITH)
L13 21 S L12 NOT 11C

```
L14          10 S L11 NOT L13

     FILE 'HCAPLUS' ENTERED AT 15:23:45 ON 24 JUN 2003
L15        2799 S L13
L16        3247 S METOPROLOL OR BEATROLOL OR SPESICOR OR CGP2175 OR CGP 2175
L17        3560 S L15,L16
                E ALEXANDER J/AU
L18         320 S E3,E8-E10
                E ALEXANDER JOHN/AU
L19          29 S E3,E10-E12
                E SCHUH J/AU
L20          53 S E3,E6,E14,E17,E18,E21,E22
L21           1 S L17 AND L18-L20

     FILE 'REGISTRY' ENTERED AT 15:25:56 ON 24 JUN 2003
L22           1 S EPLERENONE/CN
L23          36 S 107724-20-9/CRN

     FILE 'HCAPLUS' ENTERED AT 15:27:15 ON 24 JUN 2003
L24          67 S L22
L25           8 S L23
L26          81 S EPLERENONE OR SC66110 OR SC()(66110 OR 66 110) OR CGP30083 OR
L27          92 S L24-L26
L28           7 S L27 AND L18-L20
L29           1 S L21 AND L28
L30           1 S US20020123485/PN
                E WO2001-US23670/AP,PRN
L31           1 S E3,E4
                E US2000-221365/AP,PRN
L32           1 S E5
L33           1 S L29-L32
                SEL RN

     FILE 'REGISTRY' ENTERED AT 15:29:09 ON 24 JUN 2003
L34          80 S E1-E80
L35           2 S L34 AND L22,L23
L36           1 S L34 AND L13
L37          16 S L34 AND NR>=5
L38          12 S L34 AND NR>=6
L39          16 S L37,L38
L40          63 S L34 NOT L35-L39
L41           3 S L39 AND K/ELS
L42          11 S L38 NOT L41
L43          10 S L42 AND 1/NC
L44             STR
L45          50 S L44
L46             STR L44
L47          18 S L46
L48             STR L46
L49          50 S L48
L50             SCR 1851
L51          50 S L48 AND L50
L52        1341 S L48 AND L50 FUL
                SAV L52 QAZI917/A
L53             STR
L54          22 S L53 SAM SUB=L52
L55          10 S L34 AND L52
L56           6 S L39 NOT L55
L57         554 S L53 FUL SUB=L52
                SAV L57 QAZI917A/A
L58         552 S L57 NOT (CCS OR RIS OR PMS)/CI

     FILE 'HCAPLUS' ENTERED AT 15:52:30 ON 24 JUN 2003
```

```
L59          67 S L55
L60           4 S L59 AND L17

     FILE 'REGISTRY' ENTERED AT 15:53:12 ON 24 JUN 2003
L61           5 S L56 NOT C24H32O4S

     FILE 'HCAPLUS' ENTERED AT 15:53:50 ON 24 JUN 2003
L62           2 S L61
L63           1 S L62 AND L17
L64           4 S L27 AND L17
L65           4 S L33,L60,L63,L64
L66         360 S L58
L67           4 S L66 AND L17
L68           4 S L65,L67

     FILE 'REGISTRY' ENTERED AT 15:56:48 ON 24 JUN 2003

     FILE 'HCAPLUS' ENTERED AT 15:57:22 ON 24 JUN 2003

     FILE 'MEDLINE' ENTERED AT 15:57:55 ON 24 JUN 2003
L69        4457 S L17
L70          75 S L27
L71           1 S L69 AND L70
L72           5 S EPOXYMEXRENONE
L73           1 S L69 AND L72
L74           1 S L71,L73

     FILE 'EMBASE' ENTERED AT 15:59:01 ON 24 JUN 2003
L75       13961 S L17
L76         146 S L27 OR L72
L77           8 S L75 AND L76
L78         787 S L17(L)CB/CT
L79          24 S L76(L)CB/CT
L80           0 S L77 AND L78,L79

     FILE 'WPIX' ENTERED AT 16:01:38 ON 24 JUN 2003
L81         184 S L16/BIX
                E METOPROLOL/DCN
                E E3+ALL
L82         134 S E2
L83          63 S E4
L84          11 S E6
L85          12 S E8
L86          24 S E10
L87           1 S E12
L88           3 S E14
L89         242 S L81-L88
L90          20 S L26/BIX
L91           3 S L72/BIX
                E EPLERENONE/DCN
                E EPOXYMEXRENONE/DCN
L92           3 S L89 AND L90,L91

=> fil medline
FILE 'MEDLINE' ENTERED AT 16:05:34 ON 24 JUN 2003

 FILE LAST UPDATED: 21 JUN 2003 (20030621/UP).  FILE COVERS 1958 TO DATE.

 On April 13, 2003, MEDLINE was reloaded.  See HELP RLOAD for details.

 MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
 MeSH 2003 vocabulary.  See http://www.nlm.nih.gov/mesh/changes2003.html
 for a description on changes.
```

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d all l74

L74 ANSWER 1 OF 1 MEDLINE
AN 2000501947 MEDLINE
DN 20503076 PubMed ID: 11048403
TI [Cardiology at the end of the 20th century].
Kardiologie na konci 20. stoleti.
AU Jerie P
SO CASOPIS LEKARU CESKYCH, (2000 Jul 19) 139 (14) 422-5.
Journal code: 0004743. ISSN: 0008-7335.
CY Czech Republic
DT Journal; Article; (JOURNAL ARTICLE)
LA Czech
FS Priority Journals
EM 200011
ED Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001121
AB In autumn 1999 results of two well-controlled studies were published that are consistent with a frequent association between Helicobacter pylori seropositivity and coronary heart disease (CHD). Concerning the therapy of CHD, attention is mainly focused on new thrombolytic agents, bypass grafting (CABG) and balloon angioplasty (PTCA). In patients with intractable angina where aggressive medical therapy was exhausted and who were no longer candidates for CABG or PTCA, transmural laser revascularisation (TMLR), enhanced external counterpulsation (EECP) and spinal cord stimulation can be considered. TMLR was shown to improve symptoms but not myocardial perfusion; the preoperative mortality accounts for 10-20%. In hypertrophic obstructive cardiomyopathy, alcohol-induced transmural septal myocardial ablation (PTSMA) reduces both the symptoms and the left ventricular outflow tract gradient. Although the prevalence of hypertension emergencies has dramatically diminished, the number of hypertensive patients with heart failure and end-stage renal disease is increasing. It is important to detect and treat mild hypertensives in early stages, especially diabetics and younger women with additional risk factors and/or proteinuria. The choice and dosage of drugs is to be individualised. In chronic heart failure (CHF), the protective effect of ACE inhibitors, **metoprolol** and carvedilol has been repeatedly shown in CHF stage NYHA II and III. The merit of ACE inhibitor and beta-blockers in high doses remains questionable in old patients and those with severe CHF (NYHA IV). In the latter indication, spirolactone was successfully reintroduced. **Eplerenone** (**epoxymexrenone**) is a new aldosterone antagonist with little affinity to other steroid receptors and has therefore less undesirable effects than spirolactone. The body of knowledge in therapeutic and technical progress in medicine of the 20th century are summarised and their positive and negative consequences briefly discussed.
CT Check Tags: Human
*Cardiology
English Abstract

=> fil embase
FILE 'EMBASE' ENTERED AT 16:05:50 ON 24 JUN 2003

FILE COVERS 1974 TO 19 Jun 2003 (20030619/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d all tot l77

L77 ANSWER 1 OF 8 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
AN 2003214503 EMBASE
TI New developments in the pharmacological treatment of chronic heart failure.
AU Krum H.; Liew D.
CS Dr. H. Krum, NH/MRC Ctr. Clin. Res. Excellence, Department of Medicine, Monash Univ. Ctrl./E. Clin. School, Melbourne, Vic. 3004, Australia. henry.krum@med.monash.edu.au
SO Expert Opinion on Investigational Drugs, (1 May 2003) 12/5 (751-757). Refs: 57
ISSN: 1354-3784 CODEN: EOIDER
CY United Kingdom
DT Journal; General Review
FS 005 General Pathology and Pathological Anatomy
018 Cardiovascular Diseases and Cardiovascular Surgery
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LA English
SL English
AB In recent years, rapid growth in the understanding of the pathophysiology of chronic heart failure has allowed for insights into many potential new therapeutic strategies. Yet until now, despite sound biological basis for efficacy and success in early-Phase studies, novel agents have not stood up to the scrutiny of late-Phase clinical trials. Indeed, remarkably negative results have been observed for vasopeptidase inhibitors, endothelin receptor antagonists and agents which block immune activation. However, efficacy data from other novel agents are still awaited, including the selective aldosterone receptor antagonist **eplerenone**, arginine vasopressin inhibitors, erythropoietin and hydroxy-methyl-glutaryl coenzyme A reductase inhibitors. Other classes of drugs which may enter clinical development include cardiac metabolic agents, matrix metalloproteinase inhibitors and advanced glycation end product antagonists. That the mortality and morbidity of patients with chronic heart failure remain unacceptably high makes the ongoing commitment to exploration of new drug therapies for the condition critical.
CT Medical Descriptors:
*heart failure: DT, drug therapy
*heart failure: ET, etiology
pathophysiology
drug efficacy
mortality
morbidity
heart muscle metabolism
enzyme inhibition
beta adrenergic receptor blocking
immunosuppressive treatment
drug synthesis
gynecomastia: SI, side effect
angioneurotic edema: SI, side effect
body weight disorder: SI, side effect
chronic disease
human
nonhuman
clinical trial
review
Drug Descriptors:

*cardiovascular agent: CT, clinical trial
*cardiovascular agent: DV, drug development
*cardiovascular agent: PD, pharmacology
vasopeptidase inhibitor: AE, adverse drug reaction
vasopeptidase inhibitor: CT, clinical trial
vasopeptidase inhibitor: CM, drug comparison
vasopeptidase inhibitor: DT, drug therapy
vasopeptidase inhibitor: PD, pharmacology
endothelin receptor antagonist: AE, adverse drug reaction
endothelin receptor antagonist: CT, clinical trial
endothelin receptor antagonist: CM, drug comparison
endothelin receptor antagonist: DO, drug dose
endothelin receptor antagonist: DT, drug therapy
endothelin receptor antagonist: PD, pharmacology
aldosterone antagonist: AE, adverse drug reaction
aldosterone antagonist: CT, clinical trial
aldosterone antagonist: CB, drug combination
aldosterone antagonist: CM, drug comparison
aldosterone antagonist: DT, drug therapy
aldosterone antagonist: PD, pharmacology
eplerenone: AE, adverse drug reaction
eplerenone: CT, clinical trial
eplerenone: CM, drug comparison
eplerenone: DT, drug therapy
eplerenone: PD, pharmacology
argipressin: CT, clinical trial
argipressin: DT, drug therapy
argipressin: PD, pharmacology
erythropoietin: CT, clinical trial
erythropoietin: DT, drug therapy
erythropoietin: PD, pharmacology
hydroxymethylglutaryl coenzyme A reductase inhibitor: CT, clinical trial
hydroxymethylglutaryl coenzyme A reductase inhibitor: DT, drug therapy
hydroxymethylglutaryl coenzyme A reductase inhibitor: PD, pharmacology
matrix metalloproteinase inhibitor: DV, drug development
matrix metalloproteinase inhibitor: PD, pharmacology
advanced glycation end product: DV, drug development
advanced glycation end product: PD, pharmacology
dipeptidyl carboxypeptidase inhibitor: CT, clinical trial
dipeptidyl carboxypeptidase inhibitor: CB, drug combination
dipeptidyl carboxypeptidase inhibitor: CM, drug comparison
dipeptidyl carboxypeptidase inhibitor: DT, drug therapy
dipeptidyl carboxypeptidase inhibitor: PD, pharmacology
spironolactone: AE, adverse drug reaction
spironolactone: CT, clinical trial
spironolactone: CB, drug combination
spironolactone: CM, drug comparison
spironolactone: DT, drug therapy
spironolactone: PD, pharmacology
beta adrenergic receptor blocking agent: CM, drug comparison
beta adrenergic receptor blocking agent: DT, drug therapy
beta adrenergic receptor blocking agent: PD, pharmacology
carvedilol: CT, clinical trial
carvedilol: CB, drug combination
carvedilol: CM, drug comparison
carvedilol: DT, drug therapy
carvedilol: PD, pharmacology
metoprolol: CT, clinical trial
metoprolol: CM, drug comparison
metoprolol: DT, drug therapy
metoprolol: PD, pharmacology
enalapril: CT, clinical trial
enalapril: CB, drug combination

enalapril: CM, drug comparison
enalapril: DT, drug therapy
enalapril: PD, pharmacology
nebivolol: CT, clinical trial
nebivolol: DT, drug therapy
nebivolol: PD, pharmacology
valsartan: CT, clinical trial
valsartan: DT, drug therapy
valsartan: PD, pharmacology
omapatrilat: AE, adverse drug reaction
omapatrilat: CM, drug comparison
omapatrilat: DT, drug therapy
omapatrilat: PD, pharmacology
bosentan: AE, adverse drug reaction
bosentan: CT, clinical trial
bosentan: DO, drug dose
bosentan: DT, drug therapy
bosentan: PD, pharmacology
enrasentan: AE, adverse drug reaction
enrasentan: CT, clinical trial
enrasentan: CM, drug comparison
enrasentan: DT, drug therapy
enrasentan: PD, pharmacology
darusentan: AE, adverse drug reaction
darusentan: CT, clinical trial
darusentan: CM, drug comparison
darusentan: DT, drug therapy
darusentan: PD, pharmacology
endothelin converting enzyme inhibitor: DV, drug development
recombinant tumor necrosis factor alpha: AE, adverse drug reaction
recombinant tumor necrosis factor alpha: CT, clinical trial
recombinant tumor necrosis factor alpha: CM, drug comparison
recombinant tumor necrosis factor alpha: DT, drug therapy
recombinant tumor necrosis factor alpha: PD, pharmacology
etanercept: AE, adverse drug reaction
etanercept: CT, clinical trial
etanercept: CM, drug comparison
etanercept: DT, drug therapy
etanercept: PD, pharmacology
infliximab: AE, adverse drug reaction
infliximab: CT, clinical trial
infliximab: CM, drug comparison
infliximab: DT, drug therapy
infliximab: PD, pharmacology
conivaptan: CT, clinical trial
conivaptan: DT, drug therapy
conivaptan: PD, pharmacology
rosuvastatin: CT, clinical trial
rosuvastatin: DT, drug therapy
rosuvastatin: PD, pharmacology
etomoxir: CT, clinical trial
etomoxir: DV, drug development
etomoxir: DT, drug therapy
etomoxir: PD, pharmacology
unindexed drug

RN (**eplerenone**) **107724-20-9**; (argipressin) 113-79-1; (erythropoietin) 11096-26-7; (spironolactone) 52-01-7; (carvedilol) 72956-09-3; (**metoprolol**) **37350-58-6**; (enalapril) 75847-73-3; (nebivolol) 99200-09-6; (valsartan) 137862-53-4; (omapatrilat) 167305-00-2; (bosentan) 147536-97-8, 157212-55-0; (enrasentan) 167256-08-8, 183507-63-3; (darusentan) 171714-84-4; (etanercept) 185243-69-0, 200013-86-1; (infliximab) 170277-31-3; (conivaptan) 168626-94-6, 210101-16-9; (rosuvastatin) 147098-18-8, 147098-20-2;

(etomoxir) 82258-36-4

L77 ANSWER 2 OF 8 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
AN 2003077160 EMBASE
TI The pharmacological management of heart failure: Too many treatments?.
AU Van Veldhuisen D.J.; Van Gilst W.H.
CS D.J. Van Veldhuisen, Department of Cardiology, Thoraxcenter, University Hospital Groningen, P.O. Box 30.001, 9700 RB Groningen, Netherlands
SO European Journal of Heart Failure, (2003) 5/1 (5-8).
Refs: 36
ISSN: 1388-9842 CODEN: EJHFFS
PUI S 1388-9842(02)00159-9
CY Netherlands.
DT Journal; Editorial
FS 018 Cardiovascular Diseases and Cardiovascular Surgery
037 Drug Literature Index
038 Adverse Reactions Titles
LA English
CT Medical Descriptors:
*heart failure: DT, drug therapy
heart hemodynamics
mortality
enzyme inhibition
drug mechanism
drug efficacy
clinical research
side effect: SI, side effect
human
clinical trial
meta analysis
editorial
priority journal
Drug Descriptors:
*digoxin: CT, clinical trial
*digoxin: DT, drug therapy
*diuretic agent: CT, clinical trial
*diuretic agent: DT, drug therapy
*dipeptidyl carboxypeptidase inhibitor: CT, clinical trial
*dipeptidyl carboxypeptidase inhibitor: DT, drug therapy
*enalapril: CT, clinical trial
*enalapril: DT, drug therapy
phosphodiesterase inhibitor: CT, clinical trial
phosphodiesterase inhibitor: DT, drug therapy
milrinone: CT, clinical trial
milrinone: DT, drug therapy
enoximone: CT, clinical trial
enoximone: DT, drug therapy
calcium sensitizer: CT, clinical trial
calcium sensitizer: DT, drug therapy
pimobendan: CT, clinical trial
pimobendan: DT, drug therapy
calcium antagonist: CT, clinical trial
calcium antagonist: DT, drug therapy
felodipine: CT, clinical trial
felodipine: DT, drug therapy
amlodipine: CT, clinical trial
amlodipine: DT, drug therapy
dopamine receptor stimulating agent: CT, clinical trial
dopamine receptor stimulating agent: DT, drug therapy
ibopamine: CT, clinical trial
ibopamine: DT, drug therapy
vasodilator agent: CT, clinical trial
vasodilator agent: DT, drug therapy

flosequinan: CT, clinical trial
flosequinan: DT, drug therapy
prostacyclin: CT, clinical trial
prostacyclin: DT, drug therapy
beta adrenergic receptor blocking agent: CT, clinical trial
beta adrenergic receptor blocking agent: DT, drug therapy
bisoprolol: CT, clinical trial
bisoprolol: DT, drug therapy
metoprolol: CT, clinical trial
metoprolol: DT, drug therapy
angiotensin receptor antagonist: CT, clinical trial
angiotensin receptor antagonist: DT, drug therapy
losartan: CT, clinical trial
losartan: DT, drug therapy
captopril: CT, clinical trial
captopril: DT, drug therapy
valsartan: CT, clinical trial
valsartan: DT, drug therapy
aldosterone antagonist: CT, clinical trial
aldosterone antagonist: DT, drug therapy
spironolactone: AE, adverse drug reaction
spironolactone: CT, clinical trial
spironolactone: DT, drug therapy
eplerenone: CT, clinical trial
eplerenone: DT, drug therapy
endothelin receptor antagonist: CT, clinical trial
endothelin receptor antagonist: DT, drug therapy
vasopeptidase inhibitor: CT, clinical trial
vasopeptidase inhibitor: DT, drug therapy
unindexed drug

RN (digoxin) 20830-75-5, 57285-89-9; (enalapril) 75847-73-3; (milrinone) 78415-72-2; (enoximone) 77671-31-9; (pimobendan) 74150-27-9; (felodipine) 72509-76-3; (amlodipine) 88150-42-9; (ibopamine) 66195-31-1, 75011-65-3; (flosequinan) 76568-02-0; (prostacyclin) 35121-78-9, 61849-14-7; (bisoprolol) 66722-44-9; (**metoprolol**) **37350-58-6**; (losartan) 114798-26-4; (captopril) 62571-86-2; (valsartan) 137862-53-4; (spironolactone) 52-01-7; (**eplerenone**) **107724-20-9**

L77 ANSWER 3 OF 8 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
AN 2003004084 EMBASE
TI Update from the International Society on Hypertension in Blacks.
AU McCullough P.A.
CS Dr. P.A. McCullough, Div. Nutrition/Preventive Medicine, William Beaumont Hospital, Royal Oak, MI, United States
SO Reviews in Cardiovascular Medicine, (2002) 3/4 (192-195).
Refs: 7
ISSN: 1530-6550 CODEN: RCMEC5
CY United States
DT Journal; Conference Article
FS 006 Internal Medicine
017 Public Health, Social Medicine and Epidemiology
018 Cardiovascular Diseases and Cardiovascular Surgery
028 Urology and Nephrology
037 Drug Literature Index
LA English
CT Medical Descriptors:
*hypertension: DT, drug therapy
*hypertension: EP, epidemiology
*hypertension: PC, prevention
medical society
ethnic group
risk factor
cardiovascular risk

chronic kidney disease
cardiovascular disease: CO, complication
kidney failure
heart infarction
heart failure
heart arrest
patient care
diabetic nephropathy
renin angiotensin aldosterone system
blood pressure regulation
patient compliance
blood pressure monitoring
comorbidity
human
conference paper
Drug Descriptors:
low density lipoprotein: EC, endogenous compound
cholesterol: EC, endogenous compound
ramipril: CM, drug comparison
ramipril: DT, drug therapy
metoprolol: CM, drug comparison
metoprolol: DT, drug therapy
amlodipine: CM, drug comparison
amlodipine: DT, drug therapy
dipeptidyl carboxypeptidase inhibitor: DT, drug therapy
hydroxymethylglutaryl coenzyme A reductase inhibitor: DT, drug therapy
aldosterone receptor: EC, endogenous compound
aldosterone antagonist: DT, drug therapy
eplerenone: DT, drug therapy
placebo
aldosterone: EC, endogenous compound
renin: EC, endogenous compound
RN (cholesterol) 57-88-5; (ramipril) 87333-19-5; (**metoprolol**) **37350-58-6**; (amlodipine) 88150-42-9; (**eplerenone**) **107724-20-9**; (aldosterone) 52-39-1, 6251-69-0; (renin) 61506-93-2, 9015-94-5

L77 ANSWER 4 OF 8 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
AN 2002422728 EMBASE
TI Clinical treatment regimens for chronic heart failure: A review.
AU Gould P.A.; Kaye D.M.
CS P.A. Gould, Alfred Heart Centre, Commercial Rd., Prahran, Vic. 3181, Australia. d.kaye@alfred.org.au
SO Expert Opinion on Pharmacotherapy, (1 Nov 2002) 3/11 (1569-1576).
Refs: 56
ISSN: 1465-6566 CODEN: EOPHF7
CY United Kingdom
DT Journal; General Review
FS 017 Public Health, Social Medicine and Epidemiology
018 Cardiovascular Diseases and Cardiovascular Surgery
027 Biophysics, Bioengineering and Medical Instrumentation
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LA English
SL English
AB Chronic heart failure (CHF) is increasing in prevalence worldwide, particularly in the elderly. Accordingly, this epidemic is likely to translate into a major increase in healthcare costs. Systolic heart failure is the most common cause of CHF presentations. Although the causes vary, the most common single aetiological factor is ischaemic heart disease, which accounts for .apprx. 50% of heart failure presentations. Research into CHF pharmacotherapy has been copious, with the focus

principally centred on systolic heart failure. The evidence base for pharmacotherapy in CHF is amongst the largest currently in clinical medicine. There have been multiple trials establishing the mortality and morbidity benefits of pharmacotherapy. Amongst these, large scale trials of angiotensin-converting enzyme inhibitors, .beta.-blockers and spironolactone have provided a sound basis for evidence-based treatment approaches to the CHF patient. Recently research interest has increased in biomedical engineering with studies being performed in biventricular pacing and mechanical hearts. Early data with biventricular pacing or cardiac resynchronisation therapy is encouraging. Diastolic heart failure alone accounts for at least 20 - 40% of CHF presentations and whilst it may occur in isolation, is most commonly seen in association with systolic heart failure. In this study, we present a broad overview of the current therapeutic modalities for the management of CHF, with particular emphasis on pharmacotherapy.

CT Medical Descriptors:
*heart failure: CO, complication
*heart failure: DI, diagnosis
*heart failure: DT, drug therapy
*heart failure: EP, epidemiology
*heart failure: ET, etiology
*heart failure: SU, surgery
treatment planning
chronic disease
prevalence
epidemic
health care cost
systole
ischemic heart disease
clinical medicine
mortality
morbidity
clinical research
biomedical engineering
heart pacing
artificial heart
diastole
patient care
optimal drug dose
coughing: SI, side effect
angioneurotic edema: SI, side effect
slow release formulation
hypotension: SI, side effect
bradycardia: SI, side effect
drug bioavailability
hyperkalemia: SI, side effect
human
controlled study
aged
review
Drug Descriptors:
dipeptidyl carboxypeptidase inhibitor: AE, adverse drug reaction
dipeptidyl carboxypeptidase inhibitor: CB, drug combination
dipeptidyl carboxypeptidase inhibitor: CM, drug comparison
dipeptidyl carboxypeptidase inhibitor: DO, drug dose
dipeptidyl carboxypeptidase inhibitor: DT, drug therapy
dipeptidyl carboxypeptidase inhibitor: PD, pharmacology
beta adrenergic receptor blocking agent: AE, adverse drug reaction
beta adrenergic receptor blocking agent: CB, drug combination
beta adrenergic receptor blocking agent: DO, drug dose
beta adrenergic receptor blocking agent: DT, drug therapy
beta adrenergic receptor blocking agent: PD, pharmacology
spironolactone: AE, adverse drug reaction

spironolactone: CB, drug combination
spironolactone: CM, drug comparison
spironolactone: DO, drug dose
spironolactone: DT, drug therapy
spironolactone: PD, pharmacology
angiotensin receptor antagonist: AE, adverse drug reaction
angiotensin receptor antagonist: CB, drug combination
angiotensin receptor antagonist: CM, drug comparison
angiotensin receptor antagonist: DT, drug therapy
angiotensin receptor antagonist: PD, pharmacology
losartan potassium: CB, drug combination
losartan potassium: CM, drug comparison
losartan potassium: DT, drug therapy
losartan potassium: PD, pharmacology
captopril: CB, drug combination
captopril: CM, drug comparison
captopril: DO, drug dose
captopril: DT, drug therapy
captopril: PD, pharmacology
enalapril: CM, drug comparison
enalapril: DO, drug dose
enalapril: DT, drug therapy
lisinopril: CM, drug comparison
lisinopril: DO, drug dose
lisinopril: DT, drug therapy
ramipril: CM, drug comparison
ramipril: DO, drug dose
ramipril: DT, drug therapy
quinapril: CM, drug comparison
quinapril: DO, drug dose
quinapril: DT, drug therapy
trandolapril: CM, drug comparison
trandolapril: DO, drug dose
trandolapril: DT, drug therapy
perindopril: CM, drug comparison
perindopril: DO, drug dose
perindopril: DT, drug therapy
carvedilol: AE, adverse drug reaction
carvedilol: DO, drug dose
carvedilol: DT, drug therapy
carvedilol: PD, pharmacology
bisoprolol: DT, drug therapy
bisoprolol: PD, pharmacology
metoprolol: DO, drug dose
metoprolol: DT, drug therapy
metoprolol: PR, pharmaceutics
metoprolol: PD, pharmacology
bisoprolol fumarate: DO, drug dose
bisoprolol fumarate: DT, drug therapy
diuretic agent: AE, adverse drug reaction
diuretic agent: CB, drug combination
diuretic agent: CM, drug comparison
diuretic agent: DO, drug dose
diuretic agent: DT, drug therapy
diuretic agent: PK, pharmacokinetics
diuretic agent: PD, pharmacology
diuretic agent: IV, intravenous drug administration
loop diuretic agent: CB, drug combination
loop diuretic agent: CM, drug comparison
loop diuretic agent: DT, drug therapy
loop diuretic agent: PK, pharmacokinetics
loop diuretic agent: PD, pharmacology
thiazide diuretic agent: CB, drug combination

thiazide diuretic agent: CM, drug comparison
thiazide diuretic agent: DT, drug therapy
thiazide diuretic agent: PD, pharmacology
furosemide: CM, drug comparison
furosemide: DT, drug therapy
furosemide: PK, pharmacokinetics
furosemide: PD, pharmacology
torasemide: CM, drug comparison
torasemide: DT, drug therapy
torasemide: PK, pharmacokinetics
torasemide: PD, pharmacology
potassium sparing diuretic agent: AE, adverse drug reaction
potassium sparing diuretic agent: CB, drug combination
potassium sparing diuretic agent: CM, drug comparison
potassium sparing diuretic agent: DO, drug dose
potassium sparing diuretic agent: DT, drug therapy
potassium sparing diuretic agent: PD, pharmacology
eplerenone: AE, adverse drug reaction
eplerenone: CM, drug comparison
eplerenone: DT, drug therapy
eplerenone: PD, pharmacology
aldosterone antagonist: AE, adverse drug reaction
aldosterone antagonist: CM, drug comparison
aldosterone antagonist: DT, drug therapy
aldosterone antagonist: PD, pharmacology
digoxin: DT, drug therapy
digoxin: PD, pharmacology
cardiac glycoside: DT, drug therapy
cardiac glycoside: PD, pharmacology
hydralazine: CB, drug combination
hydralazine: CM, drug comparison
hydralazine: DT, drug therapy
hydralazine: PD, pharmacology
isosorbide dinitrate: CB, drug combination
isosorbide dinitrate: CM, drug comparison
isosorbide dinitrate: DT, drug therapy
isosorbide dinitrate: PD, pharmacology
verapamil: AE, adverse drug reaction
verapamil: DT, drug therapy
verapamil: PD, pharmacology
unindexed drug

RN (spironolactone) 52-01-7; (losartan potassium) 124750-99-8; (captopril) 62571-86-2; (enalapril) 75847-73-3; (lisinopril) 76547-98-3, 83915-83-7; (ramipril) 87333-19-5; (quinapril) 82586-55-8, 85441-61-8; (trandolapril) 87679-37-6; (perindopril) 82834-16-0; (carvedilol) 72956-09-3; (bisoprolol) 66722-44-9; (**metoprolol**) **37350-58-6**; (bisoprolol fumarate) 104344-23-2; (furosemide) 54-31-9; (torasemide) 56211-40-6; (**eplerenone**) **107724-20-9**; (digoxin) 20830-75-5, 57285-89-9; (hydralazine) 304-20-1, 86-54-4; (isosorbide dinitrate) 87-33-2; (verapamil) 152-11-4, 52-53-9

CN (1) Cozaar; (2) Captopril; (3) Toprol; (4) Zebeta; (5) Aldactone; (6) Lanoxin; (7) Calan

CO (1) Merck; (2) Bristol Myers Squibb; (3) Astra Zeneca; (4) Lederle; (6) Glaxo SmithKline; (7) Searle

L77 ANSWER 5 OF 8 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.

AN 2002386267 EMBASE

TI Heart failure: New data and guidelines.

AU Keown M.L.; Rahko P.S.

CS Dr. P.S. Rahko, G7/343 CSC, Cardiovascular Medicine Section, University of Wisconsin Hospital, 600 Highland Ave, Madison, WI 53792-3248, United States. psr@medicine.wisc.edu

SO Wisconsin Medical Journal, (2002) 101/7 (16-23).

Refs: 48
ISSN: 1098-1861 CODEN: WMJOA7
CY United States
DT Journal; General Review
FS 006 Internal Medicine
018 Cardiovascular Diseases and Cardiovascular Surgery
027 Biophysics, Bioengineering and Medical Instrumentation
037 Drug Literature Index
LA English
SL English
AB Heart failure is a common clinical problem, affecting at least 5 million Americans. There have been substantial advances in the understanding and treatment of heart failure in the last several years. We review current concepts for the evaluation and treatment of the various manifestations of patients with heart failure.
CT Medical Descriptors:
*heart failure: DI, diagnosis
*heart failure: DT, drug therapy
*heart failure: EP, epidemiology
*heart failure: ET, etiology
*heart failure: SU, surgery
*heart failure: TH, therapy
United States
clinical feature
disease course
diastolic blood pressure
systolic blood pressure
algorithm
electrocardiogram
hypertension: DT, drug therapy
heart left ventricle filling pressure
patient education
drug indication
drug contraindication
positive end expiratory pressure
intubation
defibrillator
heart transplantation
human
clinical trial
review
Drug Descriptors:
*diuretic agent: CT, clinical trial
*diuretic agent: DO, drug dose
*diuretic agent: DT, drug therapy
*diuretic agent: IV, intravenous drug administration
*vasodilator agent: DT, drug therapy
*vasodilator agent: PD, pharmacology
*hypertensive agent: DT, drug therapy
*hypertensive agent: PD, pharmacology
*aldosterone antagonist: DO, drug dose
*aldosterone antagonist: DT, drug therapy
dipeptidyl carboxypeptidase inhibitor: DO, drug dose
dipeptidyl carboxypeptidase inhibitor: DT, drug therapy
angiotensin receptor antagonist: DT, drug therapy
beta adrenergic receptor blocking agent: CB, drug combination
beta adrenergic receptor blocking agent: DO, drug dose
beta adrenergic receptor blocking agent: DT, drug therapy
calcium channel blocking agent: CB, drug combination
calcium channel blocking agent: DT, drug therapy
verapamil: DT, drug therapy
diltiazem: DT, drug therapy
digoxin: CB, drug combination

digoxin: DO, drug dose
digoxin: DT, drug therapy
digoxin: PD, pharmacology
furosemide: DT, drug therapy
furosemide: IV, intravenous drug administration
metolazone: AD, drug administration
metolazone: DT, drug therapy
torasemide: CT, clinical trial
torasemide: DT, drug therapy
glyceryl trinitrate: DT, drug therapy
nitroprusside sodium: DT, drug therapy
nesiritide: DT, drug therapy
brain natriuretic peptide: DT, drug therapy
dobutamine: DT, drug therapy
dopamine: DT, drug therapy
carvedilol: DT, drug therapy
metoprolol: DT, drug therapy
bisoprolol: DT, drug therapy
atenolol: DT, drug therapy
bucindolol: CT, clinical trial
bucindolol: DT, drug therapy
spironolactone: DO, drug dose
spironolactone: DT, drug therapy
eplerenone: DT, drug therapy

RN (verapamil) 152-11-4, 52-53-9; (diltiazem) 33286-22-5, 42399-41-7; (digoxin) 20830-75-5, 57285-89-9; (furosemide) 54-31-9; (metolazone) 17560-51-9; (torasemide) 56211-40-6; (glyceryl trinitrate) 55-63-0; (nitroprusside sodium) 14402-89-2, 15078-28-1; (nesiritide) 124584-08-3, 189032-40-4; (brain natriuretic peptide) 114471-18-0; (dobutamine) 34368-04-2, 52663-81-7; (dopamine) 51-61-6, 62-31-7; (carvedilol) 72956-09-3; (**metoprolol**) **37350-58-6**; (bisoprolol) 66722-44-9; (atenolol) 29122-68-7; (bucindolol) 71119-11-4; (spironolactone) 52-01-7; (**eplerenone**) **107724-20-9**

L77 ANSWER 6 OF 8 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
AN 2002135044 EMBASE
TI Current treatment and future directions in heart failure.
AU Wells G.; Little W.C.
CS G. Wells, Cardiology Section, Wake Forest Univ. School of Medicine, Medical Center Boulevard, Winston-Salem, NC 27157-1045, United States. wlittle@wfubmc.edu
SO Current Opinion in Pharmacology, (1 Apr 2002) 2/2 (148-153).
Refs: 43
ISSN: 1471-4892 CODEN: COPUBK
CY United Kingdom
DT Journal; Article
FS 006 Internal Medicine
018 Cardiovascular Diseases and Cardiovascular Surgery
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LA English
SL English
AB Recent research in the pathophysiology of congestive heart failure has focused on the blockade of neurohormonal systems. Large clinical trials have clearly demonstrated morbidity and mortality benefits of angiotensin-converting-enzyme inhibitors and beta blockers. Indeed, all patients with heart failure should be treated with these agents unless there is a specific contraindication otherwise. Despite this treatment, however, mortality from heart failure remains high. Current investigation is now focused on other pathophysiological mechanisms and the interruption of these pathways.
CT Medical Descriptors:

*congestive heart failure: DT, drug therapy
*congestive heart failure: ET, etiology
medical research
pathophysiology
morbidity
mortality
drug contraindication
renin angiotensin aldosterone system
drug tolerability
side effect: SI, side effect
gynecomastia: SI, side effect
nephrotoxicity: SI, side effect
angioneurotic edema: SI, side effect
human
controlled study
article
priority journal
Drug Descriptors:
*dipeptidyl carboxypeptidase inhibitor: AE, adverse drug reaction
*dipeptidyl carboxypeptidase inhibitor: CB, drug combination
*dipeptidyl carboxypeptidase inhibitor: CM, drug comparison
*dipeptidyl carboxypeptidase inhibitor: DT, drug therapy
*dipeptidyl carboxypeptidase inhibitor: PD, pharmacology
*beta adrenergic receptor blocking agent: AE, adverse drug reaction
*beta adrenergic receptor blocking agent: CB, drug combination
*beta adrenergic receptor blocking agent: DT, drug therapy
neurohormone: EC, endogenous compound
dipeptidyl carboxypeptidase: EC, endogenous compound
angiotensin receptor antagonist: AE, adverse drug reaction
angiotensin receptor antagonist: CM, drug comparison
angiotensin receptor antagonist: DT, drug therapy
angiotensin receptor antagonist: PD, pharmacology
losartan: AE, adverse drug reaction
losartan: CM, drug comparison
losartan: DT, drug therapy
losartan: PD, pharmacology
enalapril: AE, adverse drug reaction
enalapril: CB, drug combination
enalapril: CM, drug comparison
enalapril: DT, drug therapy
enalapril: PD, pharmacology
valsartan: CB, drug combination
valsartan: DT, drug therapy
valsartan: PD, pharmacology
candesartan: CB, drug combination
candesartan: CM, drug comparison
candesartan: PD, pharmacology
aldosterone antagonist: AE, adverse drug reaction
aldosterone antagonist: DT, drug therapy
aldosterone antagonist: PD, pharmacology
spironolactone: AE, adverse drug reaction
spironolactone: DT, drug therapy
spironolactone: PD, pharmacology
loop diuretic agent: DT, drug therapy
eplerenone: AE, adverse drug reaction
eplerenone: DT, drug therapy
metoprolol: CM, drug comparison
metoprolol: DT, drug therapy
metoprolol: PD, pharmacology
carvedilol: CM, drug comparison
carvedilol: DT, drug therapy
carvedilol: PD, pharmacology
bisoprolol: DT, drug therapy

bisoprolol: PD, pharmacology
beta 2 adrenergic receptor blocking agent: CM, drug comparison
beta 2 adrenergic receptor blocking agent: DT, drug therapy
beta 2 adrenergic receptor blocking agent: PD, pharmacology
bucindolol: DT, drug therapy
bucindolol: PD, pharmacology
moxonidine: PD, pharmacology
endothelin: EC, endogenous compound
endothelin receptor antagonist: AE, adverse drug reaction
endothelin receptor antagonist: DO, drug dose
endothelin receptor antagonist: DT, drug therapy
endothelin receptor antagonist: PD, pharmacology
bosentan: AE, adverse drug reaction
bosentan: DO, drug dose
bosentan: DT, drug therapy
bosentan: PD, pharmacology
endothelin converting enzyme inhibitor: CB, drug combination
endothelin converting enzyme inhibitor: DT, drug therapy
endothelin converting enzyme inhibitor: PD, pharmacology
phosphoramidon: CB, drug combination
phosphoramidon: DT, drug therapy
phosphoramidon: PD, pharmacology
pentoxifylline: DT, drug therapy
pentoxifylline: PD, pharmacology
etanercept: DT, drug therapy
etanercept: PD, pharmacology
vasopeptidase inhibitor: DT, drug therapy
vasopeptidase inhibitor: PD, pharmacology
omapatrilat: AE, adverse drug reaction
omapatrilat: CM, drug comparison
omapatrilat: DT, drug therapy
omapatrilat: PD, pharmacology
lisinopril: AE, adverse drug reaction
lisinopril: CM, drug comparison
lisinopril: DT, drug therapy
lisinopril: PD, pharmacology
unindexed drug

RN (dipeptidyl carboxypeptidase) 9015-82-1; (losartan) 114798-26-4; (enalapril) 75847-73-3; (valsartan) 137862-53-4; (candesartan) 139481-59-7; (spironolactone) 52-01-7; (**eplerenone**) **107724-20-9**; (**metoprolol**) **37350-58-6**; (carvedilol) 72956-09-3; (bisoprolol) 66722-44-9; (bucindolol) 71119-11-4; (moxonidine) 75438-57-2; (phosphoramidon) 36357-77-4; (pentoxifylline) 6493-05-6; (etanercept) 185243-69-0, 200013-86-1; (omapatrilat) 167305-00-2; (lisinopril) 76547-98-3, 83915-83-7

L77 ANSWER 7 OF 8 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
AN 2000292848 EMBASE
TI [Cardiology update 1999].
KARDIOLOGIE NA KONCI 20. STOLETI.
AU Jerie P.
CS Dr. P. Jerie, Leymenstrasse 49, CH-4153 Reinach, BL, Switzerland
SO Casopis Lekaru Ceskych, (2000) 139/14 (422-425).
Refs: 38
ISSN: 0008-7335 CODEN: CLCEAL
CY Czech Republic
DT Journal; General Review
FS 004 Microbiology
018 Cardiovascular Diseases and Cardiovascular Surgery
037 Drug Literature Index
LA Czech
SL English; Czech
AB In autumn 1999 results of two well-controlled studies were published that

are consistent with a frequent association between Helicobacter pylori seropositivity and coronary heart disease (CHD). Concerning the therapy of CHD, attention is mainly focused on new thrombolytic agents, bypass grafting (CABG) and balloon angioplasty (PTCA). In patients with intractable angina where aggressive medical therapy was exhausted and who were no longer candidates for CABG or PTCA, transmural laser revascularisation (TMLR), enhanced external counterpulsation (EECP) and spinal cord stimulation can be considered. TMLR was shown to improve symptoms but not myocardial perfusion; the preoperative mortality accounts for 10-20 %. In hypertrophic obstructive cardiomyopathy, alcohol-induced trasmural septal myocardial ablation (PTSMA) reduces both the symptoms and the left ventricular outflow tract gradient. Although the prevalence of hypertension emergencies has dramatically diminished, the number of hypertensive patients with heart failure and end-stage renal disease is increasing. It is important to detect and treat mild hypertensives in early stages, especially diabetics and younger women with additional risk factors and/or proteinuria. The choice and dosage of drugs is to be individualised. In chronic heart failure (CHF), the protective effect of ACE inhibitors, **metoprolol** and carvedilol has been repeatedly shown in CHF stage NYHA II and III. The merit of ACE inhibitor and .beta.-blockers in high doses remains questionable in old patients and those with severe CHF (NYHA IV). In the latter indication, spirolactone was successfully reintroduced. **Eplerenone** (**epoxymexrenone**) is a new aldosterone antagonist with little affinity to other steroid receptors and has therefore less undesirable effects than spirolactone. The body of knowledge in therapeutic and technical progress in medicine of the 20th century are summarised and their positive and negative consequences briefly discussed.

CT Medical Descriptors:
*Helicobacter pylori
*ischemic heart disease: DT, drug therapy
*heart failure: DT, drug therapy
serodiagnosis
coronary artery bypass graft
transluminal coronary angioplasty
revascularization
spinal cord stimulation
heart muscle perfusion
disease association
hypertension
risk factor
treatment indication
human
review
Drug Descriptors:
*dipeptidyl carboxypeptidase inhibitor: DT, drug therapy
*dipeptidyl carboxypeptidase inhibitor: PD, pharmacology
*beta adrenergic receptor blocking agent: DT, drug therapy
*beta adrenergic receptor blocking agent: PD, pharmacology
spironolactone: DT, drug therapy
spironolactone: PD, pharmacology
eplerenone: DT, drug therapy
metoprolol: DT, drug therapy
metoprolol: PD, pharmacology
carvedilol: DT, drug therapy
carvedilol: PD, pharmacology

RN (spironolactone) 52-01-7; (**eplerenone**) **107724-20-9**; (**metoprolol**) **37350-58-6**; (carvedilol) 72956-09-3

L77 ANSWER 8 OF 8 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
AN 1999281540 EMBASE
TI Recent progress in the treatment of hypertension and related disorders.
AU Cases A.

CS Dr. A. Cases, Dept. of Nephrology, Hospital Clinic, Villarroel 170, 08036 Barcelona, Spain
SO Drug News and Perspectives, (1999) 12/6 (372-377).
ISSN: 0214-0934 CODEN: DNPEED
CY Spain
DT Journal; Conference Article
FS 018 Cardiovascular Diseases and Cardiovascular Surgery
030 Pharmacology
037 Drug Literature Index
LA English
SL English
AB The 14th Annual Scientific Meeting of the American Society of Hypertension, held in New York, May 19-22, 1999, presented recent advances in the field of hypertension and related cardiovascular disorders. Presenters discussed the evidence for the beneficial effects of the use of .beta.-blockers in terms of mortality in patients with heart failure. The possible usefulness of endothelin antagonists in hypertension and heart failure was also discussed. The overall results of three phase II trials on the antihypertensive efficacy and tolerability of the dual vasopeptidase inhibitor omapatrilat were presented during the meeting. The antihypertensive effects and tolerability of members of the new class of I1 imidazoline receptor agonists (rilmenidine and moxonidine) were reviewed in a satellite symposium and an invited lecture. The beneficial use of antialdosteronic agents, such as spironolactone, in patients with severe heart failure and the recent development of more selective aldosterone receptor antagonists (SARAs), such as **eplerenone** - currently under investigation in hypertension and heart failure - were also presented during the meeting.
CT Medical Descriptors:
*hypertension: DT, drug therapy
*cardiovascular disease: DT, drug therapy
heart failure
drug efficacy
drug tolerability
drug structure
human
clinical trial
phase 2 clinical trial
meta analysis
conference paper
Drug Descriptors:
*beta adrenergic receptor blocking agent: CT, clinical trial
*beta adrenergic receptor blocking agent: AN, drug analysis
*beta adrenergic receptor blocking agent: DT, drug therapy
*endothelin receptor antagonist: AN, drug analysis
*endothelin receptor antagonist: DT, drug therapy
*endothelin receptor antagonist: PD, pharmacology
*membrane metalloendopeptidase: CT, clinical trial
*membrane metalloendopeptidase: DT, drug therapy
*membrane metalloendopeptidase: PD, pharmacology
*omapatrilat: CT, clinical trial
*omapatrilat: AN, drug analysis
*omapatrilat: DT, drug therapy
*omapatrilat: PD, pharmacology
endothelin 1: EC, endogenous compound
bosentan: AN, drug analysis
bosentan: DT, drug therapy
bosentan: PD, pharmacology
rilmenidine: AN, drug analysis
rilmenidine: DT, drug therapy
moxonidine: AN, drug analysis
moxonidine: DT, drug therapy
moxonidine: PD, pharmacology

spironolactone: CT, clinical trial
spironolactone: AN, drug analysis
spironolactone: DT, drug therapy
aldosterone antagonist: AN, drug analysis
aldosterone antagonist: DT, drug therapy
eplerenone: AN, drug analysis
eplerenone: DT, drug therapy
bucindolol: CT, clinical trial
bucindolol: DT, drug therapy
carvedilol: AN, drug analysis
carvedilol: DT, drug therapy
metoprolol: CT, clinical trial
metoprolol: AN, drug analysis
metoprolol: DT, drug therapy
bisoprolol: CT, clinical trial
bisoprolol: AN, drug analysis
bisoprolol: DT, drug therapy
RN (membrane metalloendopeptidase) 82707-54-8, 88201-55-2; (rilmenidine) 54187-04-1; (moxonidine) 75438-57-2; (spironolactone) 52-01-7; (bucindolol) 71119-11-4; (carvedilol) 72956-09-3; (**metoprolol**) **37350-58-6**; (bisoprolol) 66722-44-9

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=> d all abeq tech abex tot l92

L92 ANSWER 1 OF 3 WPIX (C) 2003 THOMSON DERWENT
AN 2003-075655 [07] WPIX
DNC C2003-019682
TI Use of new and known probucol monoester compounds for increasing high density lipoprotein cholesterol level used for treating cardiovascular diseases.
DC B05
IN LUCHOOMUN, J; SAXENA, U; SIKORSKI, J A; SUNDELL, C L
PA (LUCH-I) LUCHOOMUN J; (SAXE-I) SAXENA U; (SIKO-I) SIKORSKI J A; (SUND-I) SUNDELL C L; (ATHE-N) ATHEROGENICS INC
CYC 100

PI WO 2002087556 A2 20021107 (200307)* EN 161p A61K031-00
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW
US 2003064967 A1 20030403 (200325) A61K031-66

ADT WO 2002087556 A2 WO 2002-US12678 20020411; US 2003064967 A1 Provisional US 2001-283376P 20010411, Provisional US 2001-345025P 20011109, US 2002-122516 20020411

PRAI US 2001-345025P 20011109; US 2001-283376P 20010411; US 2002-122516 20020411

IC ICM A61K031-00; A61K031-66
ICS A61K031-255; A61K031-397; A61K031-40; A61K031-445

AB WO 200287556 A UPAB: 20030129
NOVELTY - Use of probucol monoester compounds (I) and (II) is claimed for increasing high density lipoprotein (HDL) cholesterol level or improving the functionality of circulating HDL.

DETAILED DESCRIPTION - Use of probucol monoester compounds of formula T-linker-X (I) and T-linkera-O-SO2-OR4 (II), their salts or prodrugs is claimed for increasing high density lipoprotein (HDL) cholesterol level or improving the functionality of circulating HDL.

T = a group of formula (i);

linker = (CH2)gQ(CH2)h;

linkera = (CH2)k, alkyl, lower alkyl, alkenyl, alkynyl, heterocyclyl, aryl, heteroaryl, aralkyl, heterocyclylalkyl, heteroarylalkyl, alkaryl, alkylheterocyclyl or alkylheteroaryl (all optionally substituted by at least one OH, alkyl, lower alkyl, 1-5C alkoxy, halo, NO2, amino, CN, aminocarbonyl, alkylamino or halo(1-5C)alkyl);

g = 1-3;

h = 0-3;

k = 1-10;

Q = O, S or CH2;

X = CH2COOR, COOR or CONR1R2;

R, R1, R2 = H, alkyl, lower alkyl, aryl, aralkyl or alkaryl (all optionally substituted by at least one OH, halo, alkoxy, carboxy or amino), or

R1 + R2 = 4-8 membered ring;

R4 = H, alkyl, lower alkyl, alkenyl, alkynyl, heterocyclyl, aryl, heteroaryl, aralkyl, heterocyclylalkyl, heteroarylalkyl, alkaryl, alkylheterocyclyl or alkylheteroaryl (all optionally substituted by at least one OH, alkyl, lower alkyl, 1-5C alkoxy, halo, NO2, amino, CN, aminocarbonyl, alkylamino or halo(1-5C)alkyl).

INDEPENDENT CLAIMS are also included for the following:

(1) new compounds (II), and;

(2) measuring the ability of a compound (preferably probucol monoester) to increase the level of circulating HDL cholesterol which comprises administering the compound to an animal (preferably mouse or hamster) transfected with the human apo A-1 gene and measuring the increase in human apo A-1 HDL.

ACTIVITY - Cardiant; Antiarteriosclerotic.

MECHANISM OF ACTION - None given in the source material.

USE - Used for increasing HDL cholesterol level, improving the circulating functionality of HDL and treating cardiovascular diseases e.g. atherosclerosis.

In an in vitro cell culture assay, HepG2 cells were cultured in minimum essential medium containing 10% FBS, and streptomycin (100 mu g/ml), penicillin (100 unit/ml) and glutamine (4 mM). Cells were grown for 2 days till they were 80% confluent in 6-well or 12-well plates before studies. To measure apoAI, 96-well microtiter plates were coated with a 1:1000 diluted mixture of three monoclonal antibodies against human apoAI

for 2 hours and incubated in succession with HDL3 (0 - 15 ng/well), carboxymethoxyacetic acid, mono(4-(1-((3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl)thio)-1-methyl-ethyl)-thio-2,6-bis(1,1-dimethylethyl)phenyl)ester (Ib) (test compound)/probucol (control compound), sheep polyclonal anti-apoAI serum, alkaline phosphatase-labeled rabbit anti-sheep and para-nitrophenyl phosphate (1 mg/ml in 10 mmol/l ethanolamine, 0.5 mmol/L MgCl2, pH 9.5), for 2, 1 and 1 hour respectively at 37 deg. C. The plates were washed three times between different incubations. The percentage increase apoAI HDL in HepG2 cells using the test compound/control compound was 47/-21.

ADVANTAGE - The probucol monoesters increase the (HDL-c) level and improve the functionality of circulating high density lipoprotein in a host, by increasing HDL-particle affinity for hepatic cell surface receptors or increasing the half life of apoAI-HDL by at least 20 (preferably 30, 40, 50 or 60)% without increasing serum LDLc levels or decreasing apoAI protein synthesis. The medicament increases the HDL holoprotein levels by decreasing the internalization and degradation of HDL holoproteins.

Dwg.0/7

FS CPI

FA AB; GI; DCN

MC CPI: B01-C04; B01-D02; B03-H; B06-A01; B06-D01; B06-D11; B07-A02A; B07-A02B; B07-D04C; B07-D08; B07-D09; B07-D13; B10-A08; B10-A09A; B10-A13C; B10-A13D; B10-A15; B10-A17; B10-B03B; B10-C03; B14-F01; B14-F07

TECH UPTX: 20030129

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preparation: No general preparation of (II) is given in the source material.

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Compounds: The method also comprises administering a statin comprising lovastatin, simvastatin, pravastatin, fluvastatin, atorvastatin, cerivastatin, mevastatin, velostatin, compactin, dalvastatin, fluindostatin, dihydrocompactin, rivastatin, SDZ-63,370, CI-981, HR-780, L-645,164, CL-274,471, alpha, beta and gamma tocotrienol, (3R,5S,6E)-9,9-bis(4-fluorophenyl)-3,5-dihydroxy-8-(1-methyl-1H-tetrazol-5-yl)-6,8-nonadienoic acid, L-arginine salt, (S)-4-((4-(4-fluorophenyl)-5-methyl-2-(1-methylethyl)-6-phenyl-3-pyridinyl)ethenyl)-hydroxy-phosphinyl)-3-hydroxy-butanoic acid, disodium salt, BB-476, (British biotechnology), dihydrocompactin, (4R-(4-alpha, 6beta(E)))-6-(2-(5-(4-fluorophenyl)-3-(1-methylethyl)-1-(2-pyridinyl)-1H-pyrazol-4-yl)ethenyl)tetrahydro-4-hydroxy-2H-pyran-2-one or 1H-pyrrole-1-heptanoic acid, 2-(4-fluorophenyl)-beta,delta-dihydroxy-5-(1-methylethyl)-3-phenyl-4-((phenylamino)carbonyl)-calcium salt(R-(Rasterisk,Rasterisk)).

The method also comprises administering a fibric acid derivative comprising clofibrate, fenofibrate, ciprofibrate, bezafibrate or gemfibrozil.

The method also comprises administering a saturated phytosterol or stanol comprising campestanol, cholestanol, clionastanol, coprostanol, 22,23-dihydro-brassicastanol, epicholestanol, fucostanol or stigmastanol.

The method also comprises administering a diuretic comprising hydrochlorothiazide, chlorothiazide, furosemide, bumetanide, ethacrynic acid, amiloride, triameterene, spironolactone, **eplerenone**, acetazolamide, althiazide, amanozine, ambuside, amiloride, arbutin, azosemide, bendroflumethiazide, benzthiazide, benzylhydro-chlorothiazide, butazolamide, buthiazide, chloraminophenamide, chlorazanil, chlorthalidone, clofenamide, clopamide, clorexolone, cyclopenthiazide, cyclothiazide, disulfamide, epithiazide, ethiazide, ethoxolamide, etozolin, fenquizone, furosemide, hydracarbazine, hydrochlorothiazide, hydroflumethiazide, indapamide, isosorbide, mannitol, mefruside, methazolamide, methyclothiazide, meticrane, metochalcone, metolazone, muzolimine, paraflutizide, perhexiline, piretanide, polythiazide, quinethazone, teclothiazide, ticrynafen, torasemide, triamterene, trichlormethiazide, tripamide, urea or xipamide.

The method also comprises administering an antihypertensive agent comprising an andrenergic blocker, a mixed alpha/beta andrenergic blocker, an alpha andrenergic blocker, beta andrenergic blocker, an andrenergic stimulant, an angiotensin converting enzyme (ACE) inhibitor, an angiotensin II receptor antagonist, a calcium channel blocker, a diuretic or a vasodilator. The andrenergic blocker comprises phenoxybenzamine, guanadrel, guanethidine, reserpine, terazosin, prazosin or polythiazide. The andrenergic stimulant comprises methyldopa, methyldopate, clonidine, chlorthalidone, guanfacine, guanabenz or trimethaphan. The alpha/beta andrenergic blocker comprises carvedilol or labetalol. The beta andrenergic blocker comprises propranolol, metaprolol, acebutol, alprenol, amosulal, arotinolol, atenolol, befunolol, betaxolol, bevantolol, bisoprolol, bopindolol, bucumolol, bufetolol, bufuralol, bunitrolol, buprandolol, butiridine hydrochloride, ebutofilolol, carazolol, carteolol, carvedilol, celiprolol, cetamolol, cloranolol, dilevalol, epanolol, indenolol, labetalol, levobunolol, mepindolol, metipranolol, **metoprolol**, moprolol, nadolol, nadoxolol, nebivalol, nipradilol, oxprenolol, perbutolol, pindolol, practolol, pronethalol, propanolol, sotalol, sufinalol, talindol, tertatolol, tilisolol, timolol, toliprolol or xibenolol. The alpha andrenergic blocker comprises doxazosin and phentolamine, amosulalol, arotinolold, apiprazole, doxazosin, fenspirlde, indoramin, labetalol, naftopidil, nicergoline, prazosin, tamsulosin, tolazoline, trimazosin or yohimbine. The angiotensin converting enzyme inhibitor comprises quinapril, perindopril, erbumine, ramipril, captopril, fosinopril, trandolapril, lisinopril, moexipril, enalapril, benazepril, alacepril, ceronapril, delapril, imadapril, moveltopril, spirapril or temocapril. The angiotensin II receptor antagonist comprises candesartan cilexetil, inbesartan, losartan, valsartan or eprosartan.
The calcium channel blocker comprises verampril, diltiazem, nifedipine, nimodipine, delodipine, nicardipine, isradipine, amlodipine, bepridil, clentiazem, fendiline, gallopamil, mibefradil, prenylamine, semotiadil, terodiline, verapamil, aranipine, bamidipine, benidipine, cilnidipine, efonidipine, elgodipine, felodipine, isradipine, lacidipine, lercanidipine, manidipine, nicardipine, nifendipine, nilvadipine, nimodipine, nisoldipine, nitrendipine, cinnarizine, flunarizine, lidoflazine, lomerizine, bencyclane, etafenone or perhexiline. The vasodilator comprises hydralazine, minoxidil, diazoxide, nitroprusside, aluminum nicotinate, amotriphene, bamethan, bencyclane, bendazol, benfurodil hemisuccinate, benziodarone, betahistine, bradykinin, bovincamine, bufeniode, buflomedil, butalamine, cetiedil, chloracizine, chromonar, ciclonicate, cinepazide, cinnarizine, citicoline, clobenfural, clonitrate, cloricromen, cyclandelate, diisopropylamine dichloroacetate, dilazep, dipyridamole, droprenilamine, ebumamonine, efloxate, eledoisin, erythrityl, etafenone, fasudil, fendiline, fenoxedil, floredil, flunarizine, ganglefene, hepronicate, hexesterol, hexobendine, ibudilast, ifenprodil, iloprost, inositol, isoxsuprine, itramin tosylate, kallidin, kallikrein, khellin, lidofiazine, lomerizine, mannitol, hexanitrate, medibazine, moxisylyte, nafronyl, nicametate, nicergoline, nicofuranose, nimodipine, nitroglycerin, nylidrin, papaverine, pentaerythritol tetranitrate, pentifylline, pentoxifylline, pentrinitrol, perhexilline, pimefylline, piribedil, prenylamine, propatyl nitrate, prostaglandin EI, suloctidil, tinofedrine, tolazoline, trapidil, tricromyl, trimetazidine, trolnitrate phosphate, vincamine, vinpocetine, viquidil, visnadine or xanthinol niacinate.
The method also comprises administering a cholesteryl ester transfer protein inhibitor comprising (-)-(2R,4S)-4-amino-2,2-ethyl-6-trifluoromethyl-3,4-dihydro-2H-quinoline-1-carboxylic acid ethyl ester.

ABEX UPTX: 20030129

SPECIFIC COMPOUNDS - The use of four compounds (I) i specifically claimed e.g:
pentanedioic acid , mono(4-((1-((3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl)thio)-1-methylethyl)thio)-2,6-bis(1,1-dimethylethyl)phenyl)ester (Ia).

One compound (II) is specifically claimed i.e: 4-(4-(1-((3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl)thio)-1-methylethyl)thio-2,6-bis(1,1-dimethylethyl)phenoxy)-4-oxo-1-butyl sodium sulfate (IIa).

ADMINISTRATION - The dosage is 0.1-500 (preferably 1-100) mg/kg/day orally, parenterally (including intravenously, intradermally or subcutaneously) or topically.

EXAMPLE - (4-((1-((3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl)thio)-1-methylethyl)thio)-2,6-bis(1,1-dimethylethyl)phenyl)-4-hydroxybutyrate (12.5 g) and sulfur trioxide trimethylamine complex (12.5 g) were dissolved in dimethylformamide (150 ml) and stirred at room temperature for 2 hours. It was evaporated under vacuum to give a residue which was dissolved in dichloromethane (100 ml). The solution was washed with water (2 x 30 ml) and evaporated. Chromatography (dichloromethane/methanol, 10:1, 5:1) gave 3-(4-((1-((3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl)thio)-1-methylethyl)thio)-2,6-bis(1,1-dimethylethyl)phenoxycarbonyl)propyl hydrogen sulfate. Tetrahydrofuran (200 ml) was added to this compound, sodium hydroxide (0.8 g) in water (5 ml) was added and the mixture was stirred at room temperature for 2 hours. It was evaporated and then 1N NaOH (200 ml) was added and the mixture stirred for 30 minutes. The precipitate was filtered out and dried to give 4-(4-(1-((3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl)thio)-1-methylethyl)thio-2,6-bis(1,1-dimethylethyl)phenoxy)-4-oxo-1-butyl sodium sulfate (IIa) (9.23 g).

L92 ANSWER 2 OF 3 WPIX (C) 2003 THOMSON DERWENT
AN 2001-482984 [52] WPIX
CR 2000-170974 [15]
DNC C2001-144714
TI New biphenyl sulfonamides, useful as angiotensin endothelin receptor antagonists and for treatment of e.g. hypertension, atherosclerosis, asthma and ischemia.
DC B05
IN GU, Z; MACOR, J E; MURUGESAN, N; TELLEW, J E
PA (BRIM) BRISTOL-MYERS SQUIBB CO
CYC 93
PI WO 2001044239 A2 20010621 (200152)* EN 286p C07D413-12
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2001020926 A 20010625 (200162) C07D413-12
EP 1237888 A2 20020911 (200267) EN C07D413-12
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR
ADT WO 2001044239 A2 WO 2000-US33730 20001213; AU 2001020926 A AU 2001-20926 20001213; EP 1237888 A2 EP 2000-984282 20001213, WO 2000-US33730 20001213
FDT AU 2001020926 A Based on WO 200144239; EP 1237888 A2 Based on WO 200144239
PRAI US 2000-643640 20000822; US 1999-464037 19991215; US 2000-481197 20000111; US 2000-513779 20000225; US 2000-604322 20000626
IC ICM C07D413-12
ICS A61K031-42; A61P009-12; C07D261-16; C07D401-12; C07D403-14; C07D413-14; C07D417-12; C07D487-04
AB WO 200144239 A UPAB: 20021022
NOVELTY - Biphenyl sulfonamides (I), and their enantiomers, diasteremers, salts and metabolites, are new.
DETAILED DESCRIPTION - Biphenyl sulfonamide compounds of formula (I), and their enantiomers, diasteremers, salts and metabolites, are new.
R1 = a group of formulae (a) - (o);

R2 = T or aryloxy, provided that when R1 is a group of formula (b), that R2 is not H, halo, (halo)alkyl, alkoxy, hydroxyalkyl, nitro, -(CH2)wNR19R20 or -NHSO2R22;

T = H, halo, CHO, (halo)alkyl, alkenyl, alkynyl, (halo)alkoxyalkyl, (cycloalkyl)alkyl, alkoxyalkoxy, cyano, hydroxy(alkyl), nitro, -CH(OR13)(OR14) or -(CH2)wY

R3 = heteroaryl;

R4, R5 = (hydroxy)alkyl, (hydroxy-substituted)cycloalkyl or (hydroxy-substituted)alkoxyalkyl; or

R4 and R5 together = cyclobutyl, cyclopentyl, cyclohexyl, tetrahydrofuranyl or tetrahydropyranyl (all optionally substituted with one or more OH);

R6 = (hydroxy)(halo)alkyl, (hydroxy-substituted)(cycloalkyl)alkyl, aralkyl, (hydroxy-substituted)alkoxy(alkyl) or -NR16R17;

R7 = -(CH2)w-CO2R15, -(CH2)w-(C=O)NR16R17, -(CH2)w-NR15(C=O)NR16R17, -(CH2)w-CH2OH or -(CH2)w-(C=O)R15, or tetrazolyl, oxadiazolyl or triazolyl (each optionally substituted with H, alkyl, OH or halo);

R8, R9, R9a, R10, R12 = H, halo, (hydroxy)alkyl, (cycloalkyl)(alkyl), (hetero)aryl, arylalkyl, alkylthioalkyl, alkoxy(alkyl); or

R11, R11a = H, alkoxy or together form a carbonyl;

R13, R14 = alkyl or together form a 5- or 6-membered ring;

R15, R16, R17 = H, (hydroxy)alkyl, (cycloalkyl)(alkyl), alkoxyalkyl, aralkyl, heterocycloalkyl, (hetero)aryl or -(CH2)wQ; or

R16 and R17 together = 4-6 membered heterocyclic ring;

n = 1 or 2;

w = 0, 1 or 2;

Y = heteroaryl, -COOH, -COOR18, -CONR19R20, -NR19-OR20, -NR21(C=O)R22, -NR21(C=O)NR19R20, -N(R19)-(alk)-NR21(C=O)R22, -NR21(C=O)OR18, -NR21SO2R22, -SO2R22, or a group of formulae (q), (r) or (s);

R18 - R22 = H, (halo)alkyl, alkoxyalkyl, cycloalkyl, alkenyl, alkynyl, (hetero)aryl or aralkyl; or

R19 and R20 together = 4-7 membered cycloalkyl ring;

R23, R24 = H, (cyclo)alkyl or together form a 3-7 membered ring;

Z = O, -N(R25)- or -C(R26)(R27)-;

x = 2,3 or 4;

R25, R26, R27 = H, (cyclo)alkyl or R26 and R27 together form a 3-7 membered cycloalkyl ring; and

R101 - R104 = T in which all (hetero)aryl rings are optionally substituted by H, halo, cyano, (hydroxy)alkyl, alkoxy, nitro or trifluoromethyl.

Provided that when R1 is a group of formula (a), (I) is not a compound of formula (II).

INDEPENDENT CLAIMS are also included for:

(1) a compound of formula (I) in which R3 = isoxazol-5-yl or isoxazol-3-yl (optionally substituted with 2 of alkyl or halogen, and R1 is any group such that the resulting compound demonstrates affinity (IC50) for both the AT1 receptor and ETA receptor of less than 5 mM at both receptors

(2) a pharmaceutical composition comprising (I), at least one ACE inhibitor (such as captotril, zofenopril, fosinopril, ceranapril, alacepril, enalapril, delapril, pentopril, quinapril, ramipril, or lisinopril), vasopepsidase inhibitor (such as omapatrilat or gemopatrilat), HMG CoA reductase inhibitor (such as pravastatin, lovastatin, atorvastatin, simvastatin, NK-104 or ZD-4522), anti-platelet agent (such as clopidigrel, ticlopidine, CS-747 or aspirin), anti-diabetic agent (such as biguanides or biguanide/glyburide combinations), beta-adrenergic agent (such as carvedilol or **metoprolol**) or minerocorticoid receptor antagonist (such as spironolactone or **eplerenone**).

ACTIVITY - Antiarthritic; nootropic; neuroprotective; antianginal; antiarrhythmic; antiarteriosclerotic; antiinflammatory; analgesic; cytostatic; cardiant; cerebroprotective; hepatotropic; dermatological;

ophthalmological; antidiabetic; antidiarrheic; anticonvulsant; vasotropic; litholytic; hemostatic; hypotensive; antimigraine; osteopathic; antipsoriatic; antiulcer.

MECHANISM OF ACTION - Endothelin receptor antagonist; angiotensin II receptor antagonist. Tests were carried out but no results are given.

USE - (I) are useful in the treatment of disorders related to renal, glomerular and mesangial cell function. For treatment of disorders related to paracrine and endocrine function. For treatment of endotoxemia or endotoxin shock or hemorrhagic shock. For alleviating pain associated with prostate and bone cancer. For preventing end-organ damage associated with the cell-proliferative effects of endothelin. For treatment of hypoxic and ischemic diseases (such as cardiac, renal and cerebral ischemia and reperfusion). As antiarrhythmic, antianginal, antifibrillatory, antiasthmatic, antiarteriosclerotic, and antidiarrheal agents. As adjuncts to thrombolytic therapy. For treatment of myocardial infarction, peripheral vascular disease (e.g. Raynaud's disease), cardiac hypertrophy, primary pulmonary hypertension, trauma, central nervous system vascular disorders (such as migraine, stroke and hemorrhage), central nervous system behavioural disorders, gastrointestinal diseases (such as Crohn's disease, ulcers and inflammatory bowel disease), pancreatitis and gall bladder disorders. For regulation of cell growth. For treatment of restenosis following transplantation. For therapy of congestive heart failure including inhibition of fibrosis. For treatment of sickle cell disease, liver disease, deleterious consequences of ET-producing tumors, spastic diseases of the urinary tract and bladder, hepatorenal syndrome, immunological diseases (including vasculitis) fibrosis associated with renal dysfunction, metabolic and neurological disorders, cancer, insulin-retinopathy, diabetes mellitus, neuropathy, retinopathy, epilepsy, bone remodelling, psoriasis, and chronic inflammatory diseases (such as arthritis, rheumatoid arthritis, osteoarthritis, sarcoidosis and eczematous dermatitis). For treatment of disorders involving broncoconstriction. For treatment of sexual dysfunction, Alzheimer's, senile dementia and vascular dementia.

Dwg.0/0

FS CPI

FA AB; GI; DCN

MC CPI: B05-B01E; B06-H; B07-D04B; B07-D09; B07-D13; B10-A08; B10-A17; B10-B02B; B10-C03; B14-C09; B14-E02; B14-E10; B14-F01; B14-F02B; B14-F02C; B14-F02D; B14-F03; B14-F07; B14-G02C; B14-G03; B14-H01; B14-J01; B14-J05D; B14-J07; B14-K01A; B14-K01D; B14-N01; B14-N13; B14-N16; B14-S06; B14-S07

TECH UPTX: 20010914

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preparation: (I) can be prepared by:

(1) reacting a sulfonyl-substituted phenyl bromide with an phenyl boronic acid (or ester) to form a biphenyl sulfonyl compound;

(2) converting the biphenyl sulfonyl compound into a biphenyl sulfonyl chloride; and

(3) reacting the biphenyl sulfonyl chloride compound with an aryl amine.

ABEX UPTX: 20010914

SPECIFIC COMPOUNDS - Numerous compounds of formula (I) are specifically claimed including 4'-((2-Butyl-4-oxo-1,3-diazaspiro(4.4)non-1-en-3-yl)methyl)-N-(4,5-dimethyl-3-isoxazolyl)-2'-(2-fluoroethoxymethyl)(1,1'-biphenyl)-2-sulfonamide

ADMINISTRATION - Dosage is 0.1 - 100 (preferably 0.2 - 50, more preferably 0.5 - 25) mg/kg. Administration is by any suitable means.

EXAMPLE - 4'-((2-Butyl-4-oxo-1,3-diazaspiro(4.4)non-1-en-3-yl)methyl)-2'-formyl-N-(3,4-dimethyl-5-isoxazolyl)-(1,1'-biphenyl)-2-sulfonamide (110 mg, 0.20 mmol) in dichloromethane (4 ml) was added to 4-amino-2,2-dimethylbutanoic acid hydrochloride (98 mg, 0.59 mmol) and 3 angstrom molecular sieves, followed by glacial acetic acid (35 mg, 0.59 mmol) and then sodium acetate (48 mg, 0.59 mmol). The mixture was stirred for 8

minutes and NaB(AcO)3H (124 mg, 0.59 mmol) was then added. The reaction mixture was stirred for 2 hours at room temperature, diluted with ethyl acetate and filtered through celite. The filtrate was washed with water and brine, dried and concentrated.. This material was dissolved in dichloromethane (6 ml) and 1,3-diisopropylcarbodiimide (32 mg, 0.25 mmol) was added. The reaction mixture was stirred at room temperature for 2 hours, diluted with DCM, washed with water and brine, dried and concentrated. The residue was purified by preparative HPLC to provide 4'-((2-Butyl-4-oxo-1,3-diazaspiro(4.4)non-1-en-3-yl)methyl)-N-(3,4-dimethyl-5-isoxazolyl)-2'-((3,3-dimethyl-2-oxo-1-pyrrolidinyl)methyl)(1,1'-biphenyl)-2-sulfonamide (40 mg, 31%), m. pt 104 - 110 degrees C.

DEFINITIONS - Preferred definitions:
R1 = a group of formulae (a), (e) or (g);
R2 = -CH2Y or (halo)(alkoxy)alkyl;
Y = a group of formula (q);
R3 = isoxazol-5-yl or isoxazol-3-yl (both substituted with two substituents selected from halo and alkyl); and
R101 - R104 = H, halo or alkyl.

L92 ANSWER 3 OF 3 WPIX (C) 2003 THOMSON DERWENT
AN 2000-317820 [27] WPIX
DNC C2000-096186
TI Treating weight loss due to cachexia which occurs in liver cirrhosis, cardiac cachexia involves administering an agent which reduces sympathetic nervous system activity and/or improves cardiovascular reflex status.
DC B05
IN ANKER, S D; COATS, A J S
PA (IMCO-N) IMPERIAL COLLEGE INNOVATIONS LTD
CYC 21
PI WO 2000021509 A2 20000420 (200027)* EN 72p A61K031-00
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: JP US
EP 1121111 A2 20010808 (200146) EN A61K031-165
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
JP 2002527378 W 20020827 (200271) 74p A61K045-00
ADT WO 2000021509 A2 WO 1999-GB3302 19991015; EP 1121111 A2 EP 1999-947762 19991015, WO 1999-GB3302 19991015; JP 2002527378 W WO 1999-GB3302 19991015, JP 2000-575485 19991015
FDT EP 1121111 A2 Based on WO 200021509; JP 2002527378 W Based on WO 200021509
PRAI GB 1999-17181 19990723; GB 1998-22458 19981015; GB 1998-22459 19981015
IC ICM A61K031-00; A61K031-165; A61K045-00
ICS A61K031-14; A61K031-167; A61K031-198; A61K031-403; A61K031-404; A61K031-4164; A61K031-4178; A61K031-433; A61K031-439; A61K031-485; A61K031-517; A61K031-56; A61K031-585; A61K031-663; A61K038-00; A61K038-55; A61K041-00; A61K045-06; A61P001-16; A61P003-10; A61P009-04; A61P009-12; A61P011-00; A61P013-12; A61P031-00; A61P031-18; A61P035-00
AB WO 200021509 A UPAB: 20000606
NOVELTY - Treating weight loss due to an underlying disease in a patient comprises administering an agent (I) which reduces sympathetic nervous system activity and/or improves cardiovascular reflex status.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) treating weight loss due to an underlying disease in a patient which involves administering any one of the following compounds (III): a compound which inhibits the effect of aldosterone such as an aldosterone antagonist; a chymase inhibitor; a cathepsin inhibitor; a beta receptor blocker; an imidazoline receptor antagonist; a centrally acting alpha receptor antagonist; a peripherally acting alpha receptor antagonist; a ganglion blocking agent; a drug that has an effect on cardiovascular reflexes and thereby reduce SNS activity such as an opiate; scopolamine;

endothelin receptor antagonist; a xanthine oxidase inhibitor; or erythropoietin;

(2) treating weight loss due to underlying disease in a patient which involves electrically stimulating the patient's muscles;

(3) use of the above mentioned compounds in the manufacture of a medicament for preventing or treating weight loss due to underlying disease (idiopathic cachexia) or aging in a patient and also for manufacture of an agent for enhancing exercise performance in a healthy individual;

(4) preventing or treating weight loss due to the aging process in the patient which involves administering an agent (I) which reduces sympathetic nervous system activity, or (III);

(5) preventing or treating weight loss due to aging process which involves electrically stimulating the patient's muscles;

(6) enhancing exercise performance in a patient by administering (I) which reduces sympathetic nervous system activity, or (III);

(7) enhancing exercise performance in a patient by which involves electrically stimulating the patient's muscles;

(8) preventing weight loss consequent to a cardiovascular disorder in a patient at risk of heart disease which involves administering (III) with an inhibiting effect on aldosterone; a beta receptor blocker; an imidazoline receptor antagonist; a centrally acting alpha receptor agonist; a peripherally acting alpha receptor antagonist; or a ganglion blocking agent.

ACTIVITY - Anabolic.

The biological activity of (III) was tested in human cachexia patients. A patient with cachexia due to chronic heart failure (CHF) and a second patient with CHF and a muscle myopathy suffering from idiopathic cachexia were treated with 50 mg of an angiotensin II receptor antagonist (losartan) daily. The clinical status and parameters of body composition, strength and treadmill exercise capacity at base line and during follow-up was study for 126 days in patient 1 and 83 days in patient 2. The results showed that in both patients the exercise capacity was improved during the study. Also patient 1 had a weight gain of 4.6 kg.

MECHANISM OF ACTION - Sympathetic nervous system activator; Cardiac reflex status enhancer (claimed).

USE - The method is useful for treating weight loss in a patient having idiopathic cachexia with an underlying disease such as AIDS, liver cirrhosis, chronic obstructive pulmonary disease with or without emphysema, chronic renal failure, chronic infections, cancer, heart disease including hypertension and chronic heart failure (claimed).

Dwg.0/5

FS CPI

FA AB; DCN

MC CPI: B01-B03; B01-C05; B04-A04; B04-C01A; B04-C01B; B04-C01C; B04-C01F; B04-N04B; B05-B01G; B06-A01; B06-A02; B06-A03; B06-D01; B06-D02; B06-D06; B06-D09; B06-D13; B06-F01; B06-F05; B07-A03; B07-D03; B07-D09; B07-D12; B07-E01; B07-E03; B07-F03; B09-B; B10-A13D; B10-A17; B10-A21; B10-B01A; B10-B02E; B10-B02F; B10-B02G; B10-B03B; B10-B04B; B14-E11; B14-J02C

TECH UPTX: 20000606

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Compounds: Compound (I) which reduces the sympathetic nervous system activity is one of the compounds (III). The compound which inhibits the effect of aldosterone is any one of spironolactone, testolactone, RU40555, RU26752, canrenoate, **eplerenone**, 3-(17beta-hydroxy-3-oxoandrosta-1,4,6,11-tetraen-17alpha-yl) propionic acid gamma lactone, 3-(9-alpha-fluoro-7beta-hydroxy-3-oxo-androsta-4-en-17alpha-yl) propionic acid gamma lactone, dihydro-spirorenone, spirorenone, 15,16-methylene derivatives of spironolactone, mespirenone and SC9420. The chymase inhibitor is any one of alendronate, aprotinin and tissue inhibitors of matrix metalloproteinases. Cathepsin B inhibitor is any one of an epxoxysuccinyl peptide such as CA-074 or E64-c, stefin A and cystatin C. beta-receptor

blocker is any one of acebutolol, alprenolol, atenolol, betaxolol, bisoprolol, carteolol, celiprolol, esmolol, labetolol, lavobunolol, metipranolol, **metoprolol**, nadolol, oxprenolol, penbutolol, pindolol, propanolol, sotalal, timolol, nebivolol, carvedilol and bucindolol. Imidazoline receptor antagonist is any one of moxonidine, rilmenidine, pentamidine and alpha-methyl DOPA. Centrally acting alpha receptor agonist is clonidine. Peripherally acting alpha receptor antagonist is any one of doxazosin, prazosin, terazosin and ipsapirone. Ganglion blocking agent is any one of azamethonium, dicolinium, hexamethonium, mecamylamine, pentamethonium, pentolinium, trimetaphan, benzohexonium, hexafluorenium, cypenam, trimethaphan canfosulfonate, tetraethylammonium bromide and synapleg. Opiate is any one of dihydrocodeine, morphine, diamorphine and buprenorphine. ET-1 receptor antagonist is any one of butenolide, BQ123, BQ-788, A-216546, ABT-627, IRL3461, LU135252, S-0139, PD 142,893,PD 164333, RO 61-1790, PD 156,707, SB 209670, IRL 1038 AND WS-7338 B. Xanthine oxidase inhibitor is any one of allopurinol, 7,8-dihydroneopterin, 5,6,7,8-tetrahydrobiopterin, leukopterin, xanthopterin, neopterin, biopterin, 4-amino-6-hydroxypyrazolo(3,4-d)pyrimidine (AHPP) and oxypurinol.

ABEX UPTX: 20000606

ADMINISTRATION - Administration is through oral, parenteral injections, through inhalation, per-rectal and buccal routes. No specific clinical dosages are given.

EXAMPLE - No relevant example given.